VOL. X. (No. 2) AUGUST, 1957

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY

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ISSUED BY THE BRITISH MEDICAL ASSOCIATION
LONDON: BRITISH MEDICAL ASSOCIATION HOUSE
TAVISTOCK SQUARE, W.C.1

Published Quarterly Subscription 25s. per annum; U.S.A. $6.00 Price 7s. 6d.

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Brown, A. B. (1945). *Rev. Neurol.*, **16**, 427.

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ANGIOMATOSE ENCÉPHALO-TRIGÉMINÉE (STURGE-WEBER) SANS CALCIFICATIONS RADIOLOGIQUEMENT DÉCELABLES

(OBSERVATION ANATOMO-CLINIQUE)

PAR

C. HAEMERLINCK, GILBERT MYLE, et LUDO van BOGAERT

(RECEIVED 8TH MARCH, 1947)

LA question de la présence obligatoire ou non obligatoire des foyers de calcification intercraniens, radiologiquement décelables, dans l'angiomatose encéphalo-trigéminée, est partiellement résolue. La littérature récente contient des documents suffisamment suggestifs à cet égard. Greenwald et Koota (1936) ont publié un cas de neuro-angiomatose sans calcifications intracérébrales radiologiquement décelables. La trépanation leur a permis d'observer sous la dure-mère la présence de nappes vasculaires arachnoïdo-piales anormales. Goeters (1941) a pu faire l'examen anatomo-pathologique d'un cas semblable. Il a trouvé une angiomatose arachnoïdo-piale intéressant les deux hémisphères cérébraux mais pas de foyers de calcification.

Bien d'autres auteurs encore admettent l'existence de cas d'angiomatose encéphalo-trigéminée sans calcifications radiologiquement décelables. Marque (1927), Brushfield et Wyatt (1927), Hudelo (1929), Sillevis Smitt (1929), Bergstrand, Olivecrona, et Toennis (1936), Bebin (1945) et d'autres défendent ce point de vue. Parkes-Weber (1922) lui-même admet implicitement l'existence de tels cas. En annexe de son observation princeps, il décrit en effet deux cas, appartenant à Worster-Drought, où une angiomatose cutanée débordant au-delà du territoire radiculaire du trijumeau se trouve associée à des crises jacksoniennes intéressant l'autre moitié du corps. Mais combien justifiée fut l'intervention de Stewart à cette même séance de la section neurologique de la Royal Society of Medicine (13 décembre, 1928), lorsqu'il rapporta un cas d'angiomatose cutanée diffuse mais prédominant à la face chez un imbécile épileptique et hémiplégique dès l'enfance. A l'autopsie de ce cas Stewart n'a trouvé qu'une hémiatrophie cérébrale gauche mais pas d'angiomatose méningée ou cérébrale. L'on doit même se demander si certains des documents anatomo-cliniques d'avant l'ère radiologique ne concernent pas des cas d'hémiplégie cérébrale commune où l'on trouve la coexistence d'hémiatrophie cérébrale, de calcifications intracérébrales et d'angiome cutané facial. Pareille association fortuite ne rentre évidemment pas dans le cadre de l'angiomatose des centres nerveux.

Notre but est d'aborder ici la question du caractère obligatoire ou non obligatoire de la présence de l'angiomatose méningée et des foyers cérébraux calcifiés radiologiquement décelables et aussi souligner certaines particularités qui distinguent ce nouveau cas de tous ceux de la littérature actuellement accessibles.

Observation Clinique

M. L., 30 ans, en traitement à l'asile d'Eecloo pour oligophrénie et épilepsie.

Antécédents héréditaires.—Le père, âgé de 64 ans, atteint de crises asthmatiformes depuis 1933. Mentalement normal ; il porte quelques nævi pigmentaires pileux non verruqueux dans la partie supérieure du dos. Ouvrier brasseur, il n'a que rarement abusé de boissons éthyliques. La mère, âgée de 63 ans, bien portante mentalement, astreinte pendant des années à un travail assez dur dans une filature. Pas de cas d'affections neuro-psychiatriques ou de dystrophies notoires parmi les proches parents. Ils ont eu cinq enfants morts en bas âge. Le premier de ceux-ci est mort à trois mois d' " hydropisie." Le second, chétif, n'a vécu que quatre semaines. Les trois suivants n'ont pas atteint deux ans et ont succombé à des affections banales de l'enfance. Aucun de ces cinq enfants n'était porteur d'angiomes.

Antécédents personnels.—Notre malade est l'enfant cadet. La mère au cours de sa sixième grossesse n'a pas abandonné l'usine et s'est parfois bien fatiguée. L'accouchement a été assez difficile, mais n'a pas nécessité de recours instrumental. On ignore à quel âge la malade a fait ses premiers pas et quand elle est devenue propre. Elle fit ses premières crises convulsives à 15 mois. Ces accès se répétèrent depuis à intervalles irréguliers. Il s'agissait toujours de crises motrices généralisées. L'enfant n'a pas fréquenté l'école par suite de son oligophrénie avérée. Vers l'âge de 15 ans elle a été placée à l'Institut médico-pédagogique de

Lokeren. Nous ignorons combien d'années elle y resta. Après quelques années elle fut reprise par ses parents, mais elle entra un peu plus tard dans l'asile pour épileptiques à Eecloo.

Etat actuel (1942).—Elle est manifestement idiote ; cependant il est probable qu'un certain degré de démence s'est greffé sur le fond d'oligophrénie primitif. Elle a actuellement un âge mental de 2 ans environ. Elle ne parle pas. Sa mimique laisse percer une idéation des plus rudimentaires et certains désirs, tel celui de recevoir des caresses et des friandises. Elle est extrêmement puérile, affectueuse, et donne des caresses aux infirmières et aux autres malades. Elle est peureuse, irascible, parfois impulsive voire aggressive. Elle s'adonne à l'onichophagie et à d'autres tics, tel celui de se gratter le cuir chevelu. Du point de vue psychomoteur, elle présente un retard tout aussi considérable, mais ne gâte que rarement, probablement à l'occasion de paroxysmes comitiaux. Elle s'avère incapable de toute occupation utile.

Au point de vue somatique elle paraît avoir une tête d'adulte mais son tronc et ses membres sont ceux d'une adolescente. Son massif craniofacial est en effet bien plus développé que le reste du corps. Les taches d'angiomatose cutanée et celles des muqueuses sont très foncées, non verruqueuses mais par endroits légèrement surélevées par rapport à la peau saine environnante. Les moitiés droites des lèvres qui participent à l'angiomatose faciale sont nettement hyperplasiques. L'angiome couvre presque toute l'hémiface droite, une partie de l'hémicrâne droit, l'épaule droite, la partie supérieure de la région pectorale, la moitié latérale du bras et de l'avant-bras, la moitié latérale du dos de la main à droite, une partie de la surface dorsale des doigts, qui sont nettement plus volumineux que leurs congénères gauches (Fig. 1). A peu près tout le membre supérieur droit est plus développé que le gauche. Cette asymétrie dans le développement ne s'observe pas au niveau des membres inférieurs. La moitié gauche de la face est également envahie par l'angiome, mais les clairières de peau saine, ou à peu près saine, sont plus nombreuses que celles de l'hémiface droite : la majeure partie de la pointe du nez, d'où part une bande de 1,5 cm. de large qui passe sous la pommette gauche et gagne le pavillon de l'oreille gauche. Au niveau du cuir chevelu, au dessus du front, l'angiomatose ne dépasse pas le bregma. La région fronto-temporale droite est assez riche en éléments angiomateux, alors que la région correspondante gauche en est presque dépourvue. Les maxillaires supérieur et inférieur sont hyperplasiques, surtout dans le sens vertical. Ici surtout, l'angiome est ostéohypertrophique au sens d'Ollier, Duzéa, Parkes-Weber et d'autres. L'hémilangue droite et la moitié de la voûte palatine, couvertes d'une muqueuse angiomateuse, sont également plus développées que la moitié gauche de ces organes.

L'examen neurologique met en évidence : une légère anisoréflexie ostéotendineuse, les réflexes gauches sont un tantinet plus vifs ; les réflexes cutanés abdominaux abolis. Les signes de Babinski, d'Oppenheim, de Rossolimo et de Hoffmann sont négatifs. L'exploration systématique des fonctions sensorielles et sensitives a été impossible à cause de l'état mental de la malade. Il n'y avait en tous cas pas de grosses anomalies de ce côté. Les réflexes pupillaires sont présents. La méfiance et la peur de la malade ont rendu impossible l'exploration des fonds des yeux.

L'examen radiologique, pratiqué par le Professeur Dewitte, qui avait examiné déjà plusieurs cas d'angiomatose encéphalo-trigéminée dont certains avec réseau calcaire intracérébral, d'autres sans calcifications radiologiquement décelables, met en évidence : un crâne hyperplasique à larges sinus frontaux, une voûte anormalement épaisse et plus vascularisée surtout à gauche, une légère hypoplasie de l'hémicrâne droit, une ostéoporose diffuse du type que l'on rencontre dans les cas dits d' " angiome ostéohypertrophique " et dans bien des cas de maladie de Sturge-Weber avec foyer calcifié cérébral radiologiquement décelable. Massif maxillo-mandibulaire fortement hyperplasique. Cependant le fait de trouver, à la verification anatomique de notre cas, de nombreux foyers de calcification intracérébraux, nous a amené à réexaminer et de plus près les radiographies de notre malade. Nous avons remarqué alors que l'hémisphère cérébral droit paraissait dans son ensemble un peu plus dense que l'hémisphère gauche, et que, sur les radiographies de profil, juste en dessous de la suture lambdoïde, une ombre à peine décelable semble correspondre à un précipité de pseudochaux dans les lobes occipitaux. L'examen radiologique de tranches vertico-transversales des lobes occipitaux du cerveau fixé a mis en évidence quelques-unes des plages de calcification les plus denses, mais ne revêtant point l'aspect pseudo-vasculaire que l'on trouve habituellement dans la maladie de Sturge-Weber.

Le cœur et les poumons ne montrent pas d'anomalies cliniquement décelables. Tension artérielle 11/7 cm. Système digestif paraissant fonctionner normalement. Ni albuminurie, ni glucosurie. Menstruations régulières depuis l'âge de 16 ans. La maladie ne paraît guère évolutive au cours des dernières années de la vie de notre sujet. Une pneumonie l'emporta à l'âge de 34 ans.

Autopsie.—L'autopsie se limita à la tête, aux régions cervicale et lombosacrée et au foie. Au niveau du cou nous n'avons pas trouvé d'angiomatose des vertèbres cervicales, des méninges, de la moelle. Dans la région lombosacrée il n'y a pas de spina bifida occulta. Le foie ne contient pas de formations kystiques. Au niveau du crâne des sinus frontaux très larges (ceux de droite un peu plus vastes) et une calotte anormalement épaissie surtout à droite (Fig. 2). Un hyperdéveloppement net du réseau diploïque de la moitié droite de la calotte. Cette hyperplasie vasculaire n'est pas toujours située exactement sous l'angiomatose cutanée correspondante. L'hémicrâne droit est nettement plus petit que l'hémicrâne gauche ; les moitiés droites des deux étages antérieurs du crâne sont nettement moins excavées que les moitiés gauches. Par contre la fossette occipitale inférieure gauche est moins profonde que la fossette inférieure droite (Fig. 3). La face endocranienne de la calotte est pourvue de taches angiomateuses de tonalité très sombre rappelant la teinte bleu foncée des angiomes cutanés que porte notre malade. Elles semblent assez

éloignées des taches angiomateuses de la face exocranienne de la voûte.

La dure-mère que recouvre la moitié droite de la base du crâne est nettement plus vascularisée que celle qui recouvre la moitié gauche de la base (Fig. 4). Au moment où l'on détache cette partie de la dure-mère on s'aperçoit de ce qu'on arrache de fins éléments vasculaires qui vont de la face interne du crâne à la dure-mère. Ces minuscules vaisseaux sortent par de petits pertuis de la table interne et sont particulièrement nombreux près des trous déchirés antérieur et postérieur droits. Ils forment comme des traînées où la table interne est presque inexistante. Un nodule d'hyperostose interne de la grandeur d'un noyau de pêche est inséré sur la face endocranienne de la voûte au niveau de la partie inférieure gauche de la structure coronaire près de l'extrémité latérale de la crête osseuse qui sépare la moitié gauche des fosses antérieure et moyenne du crâne. La petite aile sphénoïdale droite est plus massive que la gauche. Certains foramina de la base sont un peu plus béants à droite qu'à gauche. Les sutures coronaires et sagittales sont presque complètement synostosées. La dure-mère présente dans toute son épaisseur, et plus particulièrement dans son tiers médian et postérieur, dans ses deux tiers juxtahémisphériques, un réseau télangiectasique très développé, plus dense au niveau de certains placards et plus important dans la partie qui recouvre les régions pariéto-occipitales droites. Deux fragments sont prélevés, l'un à droite et l'autre à gauche, pour examen histologique. La méninge molle est au niveau des régions pariétale et paracentrale droite un peu plus opalescente qu'à gauche. Elle est occupée dans toute la moitié postérieure des deux hémisphères par un réseau vasculaire très dense. Ce niveau est plus séré et plus étendu au niveau de la région temporo-occipitale droite que gauche. L'hémisphère droit apparaît sur la photographie un peu plus volumineux que le gauche, mais ce n'est qu'une apparence due à une déformation artificielle au niveau de la région pariétale et du pli courbe gauches au cours de la fixation (Fig. 5).

L'inspection du réseau veineux de la face supérieure du cerveau montre une dilatation anormale des grandes et petites veines anastomotiques surtout de la grande veine à gauche. Les veines centrales ont un aspect normal. Le réseau veineux dépendant de la petite veine anastomotique et les collatérales qui montent de celle-ci vers le sinus longitudinal supérieur est particulièrement abondant à droite ; on les prendrait pour des artères. La vascularisation duremérienne signalée plus haut est en connexion avec ce réseau. Les veines cérébelleuses ne présentent aucune particularité. La veine basilaire est également hyperplasiée. Au niveau de la face inférieure on poursuit dans la partie postérieure du lobe temporal et surtout au niveau du pôle occipital le même réseau télangiectasique, mais les veines dépendant de la cérébrale moyenne ont un calibre normal. A l'exploration digitale on perçoit une très légère induration de l'hemisphère droit mais pas de foyer calcifié cérébral.

Le cerveau est débité en coupes vertico-transversales. Malgré que les coupes ne soient pas rigoureusement transversales, on remarque aussitôt une atrophie de tout l'hémisphère droit, débutant déjà dans la région frontale moyenne et s'accentuant vers le pôle occipital, plus nette au niveau des lobes temporal et occipital et du pli courbe (Fig. 6). L'atrophie de la substance blanche centrale est fort nette. Les tranches ne crissent nulle part sous le couteau, elles sont lisses au toucher, l'axe blanc n'est pas plus induré à droite qu'à gauche. L'hémisphère cérébelleux gauche est plus petit que le droit. Le tronc cérébral est normal et symétrique.

L'examen macroscopique des centres nerveux confirme donc la présence d'un réseau télangiectasique très dense au niveau de la région pariéto-occipitale droite surtout et, à un moindre degré à gauche, en continuité avec le réseau dural, avec les veines de la diploë des os plats et les télangiectasies du cuir chevelu et de la face. Au toucher de la région occipitale et à la section du cerveau en coupes vertico-transversales, sauf une certaine induration du pôle occipital, rien n'attirerait l'attention en particulier, on ne percevait au toucher aucun grain calcifié. Tous les caractères macroscopiques du cerveau des malades atteints de la maladie de Sturge-Weber sont ici présents : atrophie en masse du parenchyme nerveux, dans tout l'hémisphère correspondant aux télangiectasies les plus développées, présence de réseaux télangiectasiques classiques, présence d'anomalies veineuses très nettes sous forme d'ectasies veineuses étendues dans le domaine des petites et des grandes veines anastomotiques.

Étude histologique.—Nous réservons pour un travail ultérieur l'étude sériée sur blocs inclus à la celloïdine et n'apporterons ici que les détails notés sur les coupes à congélation (crésyl-violet, rouge-écarlate, Spielmeyer et Holzer) et sur quelques fragments inclus à la paraffine et colorés par l'hématéine éosine et van Gieson.

La dure-mère détachée du périoste est constituée de plusieurs plans fibreux orientés en différentes directions, mais dans chaque plan fibreux on trouve de grands lacs veineux, plus abondants et plus larges que normalement ; de ci de là quelques amas constitués de cellules d'aspect endothélial. L'arachnoïde est, au niveau de son feuillet dural, occupée par un lacis veineux plus dense, à cavités moins larges. Ce réseau est plus dense et plus important à droite qu'à gauche. Le feuillet interne de l'arachnoïde est occupé par des cavités veineuses encore plus dilatées, certaines ectasies veineuses atteignant comme dimension la moitié de la circonvolution, dans les sillons desquelles on les trouve. Leur paroi est simplement fibreuse. Les artères ont leur aspect normal. Nulle part on ne voit avec certitude d'anastomoses artérioveineuses. Le pôle occipital présente au niveau de la calcarine, mais surtout au niveau des circonvolutions occipitale et temporale inférieure un début de dépôts calcaires d'intensité variable allant depuis la simple précipitation de gouttelettes à la surface d'un capillaire jusqu'à des manchons denses avec tous autour des vaisseaux constituant une carapace d'épaisseur égale à celle du calibre des vaisseaux eux-mêmes. A un stade plus avancé, la

lumière des vaisseaux est oblitérée et les grains de chaux constituent par opposition des couches nouvelles. Il y correspond, dans les Holzer, une gliose axiale dense et, dans les Spielmeyer, une démyélinisation diffuse de la substance blanche axiale des circonvolutions.

A l'examen histopathologique on voit donc que le processus de calcification de l'écorce est déjà en cours d'évolution et même fort net, malgré qu'il ne soit pas encore décelable à la radiographie. Il débute indifféremment dans les couches I et III comme le montrent les auteurs classiques sous forme de précipitations dans le tissu même, mais surtout, au niveau des capillaires sous forme de très fines granulations prenant en noir les bleus basiques devenant de plus en plus gros, puis devenant coalescentes pour constituer finalement des carapaces péri- et intrapariétales ou même des blocs de pseudo-chaux.

Nous n'avons pas l'intention de reproduire dans cette courte présentation la littérature très étendue de la maladie, mais voudrions rappeler cependant que l'observation de Kalischer, une des premières en date (1901) et des plus remarquables au point de vue de la description minutieuse de l'anatomie et même de l'histologie des lésions, ne comporte, ni macroscopiquement ni microscopiquement, de dépôts calcaires ou du moins que l'auteur ne les signale pas.

Commentaire

Ce cas se distingue de tous ceux de la littérature par la participation massive et bilatérale de la dure-mère à l'angiomatose et par la présence de précipité de pseudo-chaux dans les deux hémisphères cérébraux. La confrontation des radiographies du crâne, de celles de tranches cérébrales fixées et des données images histopathologiques démontre que de nombreuses plages de calcification intracérébrales peuvent échapper à l'examen radiologique intra vitam. En effet, les concrétions présentes dans les circonvolutions temporales inférieures n'ont pas du tout marqué ni été mises en évidence sur les radiographies de notre sujet. Sur les radiographies de face on observe une légère différence dans la densité des deux hémisphères cérébraux, mais on n'y découvre aucun foyer nettement délimité de concrétions calcaires. Cette constatation apporte un argument en faveur de la thèse de ceux qui estiment qu'il existe des cas de maladie de Sturge-Weber avec calcifications histologiquement mais non radiologiquement décelables. It est probable qu'il existe deux grandes variétés d'angiomatose systématisée du type Sturge-Weber : celle avec calcifications radiologiquement décelables, et celle où la signature radiologique des foyers calcifiés cérébraux manque.

Il s'agit donc incontestablement, dans notre cas, d'angiomatose systématisée puisque, en plus de la peau, différents plans sous-jacents y participent. Aussi estimons-nous fort probable que l'extension bilatérale de l'angiomatose centrale est en rapport avec la bilatéralité de l'angiomatose faciale. Il s'agit, au moins en partie, d'une continuité et non simplement d'une contiguité avec l'angiomatose superficielle et profonde, ainsi que le démontre la présence de nombreuses anastomoses surnuméraires, qui aident à assurer une certaine continuité entre les réseaux angiomateux des différentes enveloppes de l'encéphale. Cette continuité ne se réalise pas partout dans un sens perpendiculaire par rapport aux enveloppes du cerveau. Ainsi l'angiome facial chez notre sujet s'arrête, comme dans la plupart des cas, à hauteur de la suture, mais il semble plonger dans les plans sous-jacents et se continuer dans le réseau diploïque. Dans la diploë la télangiectasie est plutôt parallèle à la face externe du crâne, mais atteint sans doute plus loins la face endocranienne et, à certains endroits, la face externe, de la dure-mère et finalement les méninges molles.

Bien que nous ne rejetions pas à priori la possibilité d'une extension légèrement progressive des plages cérébrales calcifiées, nous avons de la peine à croire que seule la différence d'âge de notre sujet avec celui de Goeters soit responsable du fait que dans le cas de Goeters (1941) les calcifications manquent, alors que dans notre cas elles ne font pas défaut. Il est possible que Goeters ne les ait pas recherché au microscope. Les particularités de notre cas ne prouvent rien contre l'hypothèse d'après laquelle la formation des précipités calcaires serait secondaire à la sclérose cérébrale et à l'angiomatose. Nous ignorons si le nodule d'hyperostose interne greffé au niveau de l'extrémité inférieure gauche de la suture coronaire a une signification autre que celle d'une anomalie banale associée. Il est possible qu'elle soit d'origine traumatique, séquelle d'une fracture du crâne.

Comme dans la plupart des cas d'angiomatose du type Sturge-Weber, dans notre cas l'hémisphère cérébral le plus atteint est homolatéral par rapport à l'angiome facial le plus étendu et débordant au-delà du territoire radiculaire du trijumeau. Le fait que le père de notre malade soit porteur de nævi pigmentaires banaux (Koch, 1938) ne nous permet pas de conclure à l'existence chez lui d'une phacomatose authentique, il est vrai que Vanderhoeve admet qu'une telle manifestation isolée (Louis-Bar, 1944-5) justifie le diagnostic de phacomatose chez une personne appartenant à une famille où l'affection a atteint plusieurs membres. Enfin, une dernière conclusion se dégage de nos constatations anatomo-cliniques : pour des anomalies aussi peu circonscrites l'intervention chirurgicale ne peut constituer le traitement de choix.

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FIG. 1.—Photographie de la malade, vue de face.

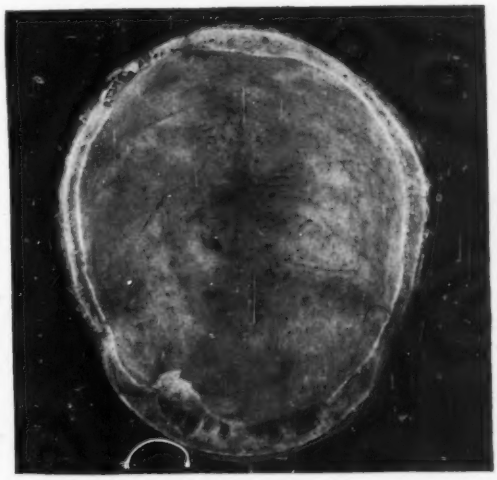


FIG. 2.—Calotte cranienne vue par la base : épaississement notable de l'hémicalotte droite dans toute son étendue.

For further illustrations to this article see overleaf

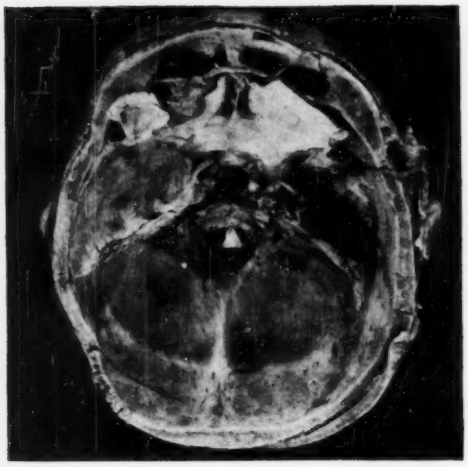


FIG. 3.—Base du crâne. Remarquer l'asymétrie de la base, la réduction de la fossette occipitale a gauche.

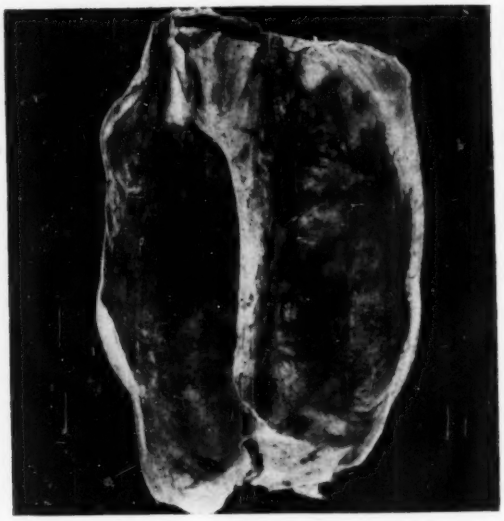


FIG. 4.—La dure-mère décollée de la calotte, vue par sa face interne ; présence de télangiectasies dans l'épaisseur de la dure-mère surtout à gauche et près de la ligne médiane.

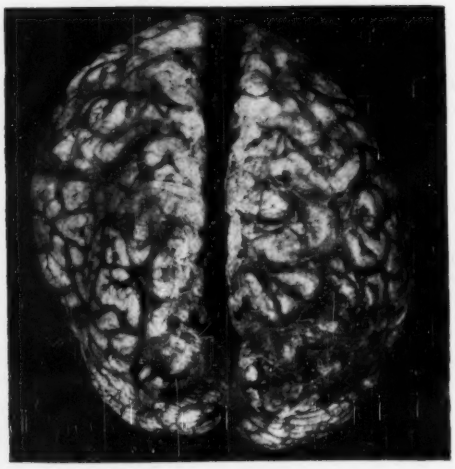


FIG. 5.—Le cerveau vu d'en haut : hémiatrophie cérébrale portant sur le pôle postérieur et antérieur ; réduction de l'hémisphère cérébelleux gauche.

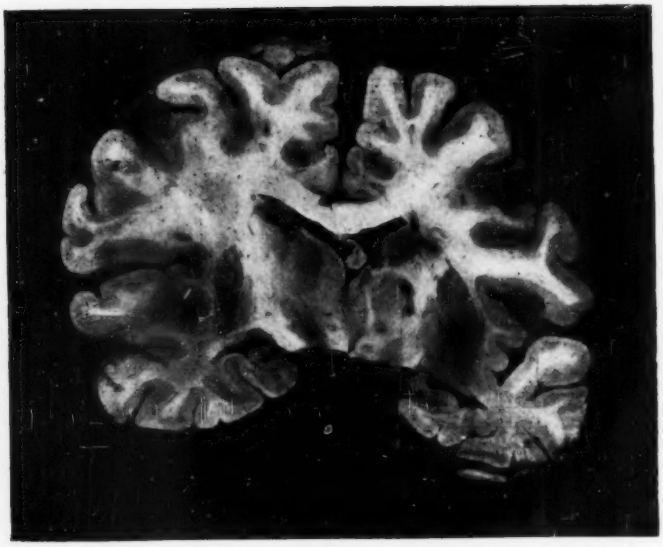
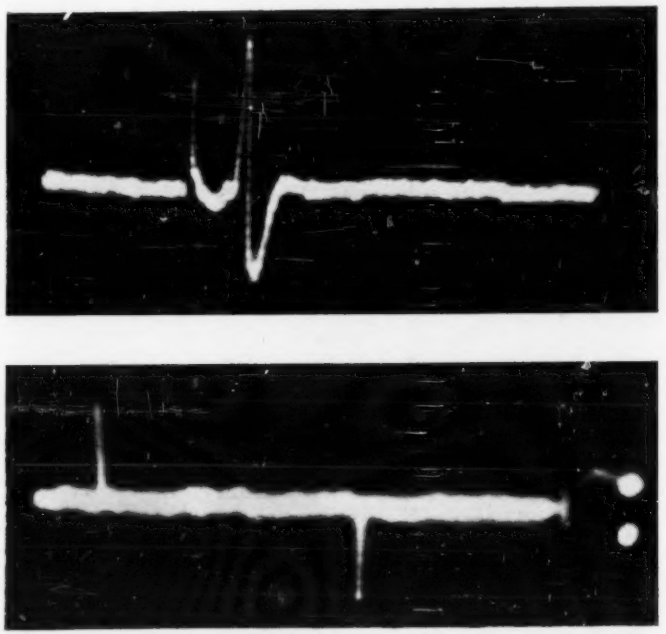


FIG. 6.—Coupe vertico-transversale du cerveau, montrant à droite la réduction de la substance blanche surtout dans le lobe temporal, l'insula et les régions motrices. Sauf le thalamus, qui est atrophié du côté homolatéral, et l'atrophie du pied, les noyaux gris centraux sont normaux.



F.G. 1

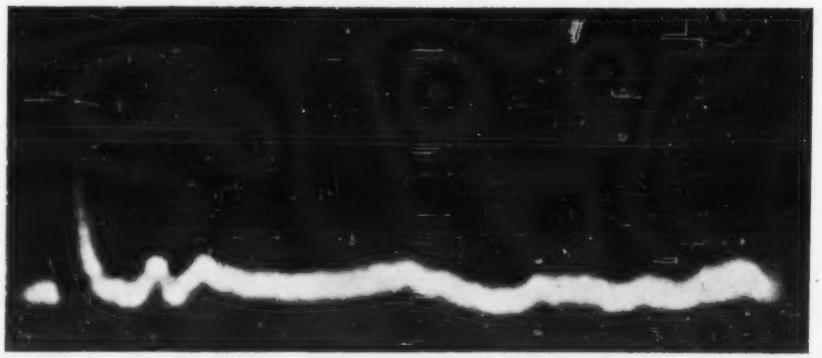


FIG. 2

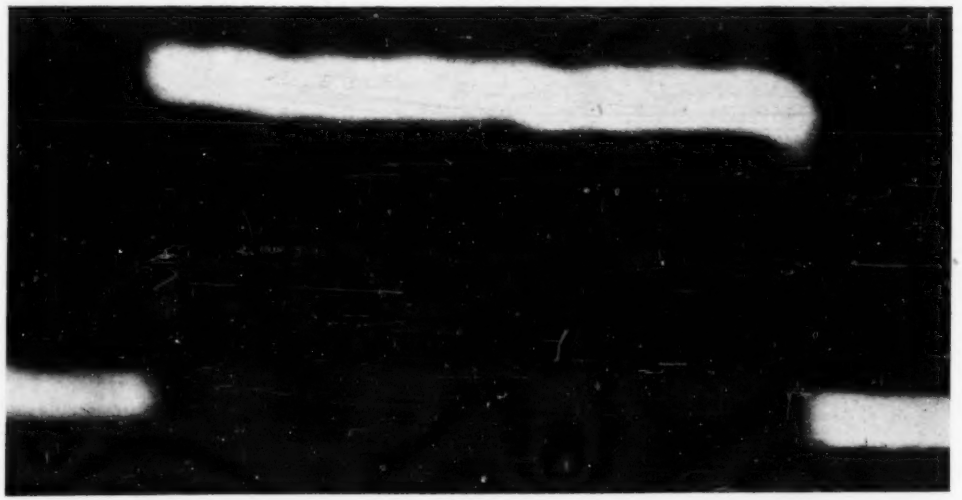
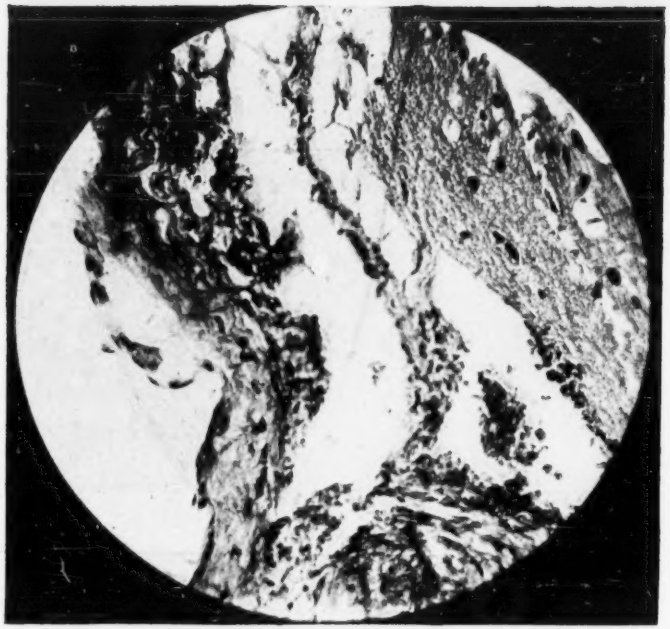


FIG. 3

FIG. 1.—The upper tracing shows the diphasic action potential recorded from the ulnar nerve at operation. The first sharp rise is the stimulus artefact. In the lower tracing, the spikes represent a calibrating voltage of 50 microvolts, the distance between the spikes being 10 milliseconds.

FIG. 2.—20 microvolt action potential recorded from electrodes below a lesion of the sciatic nerve, in which no muscular contraction resulted from maximal electrical stimulation.

FIG. 3.—A 5 millisecond stimulus derived from the stimulator employed for the testing of muscular excitability. The good square wave form is apparent.



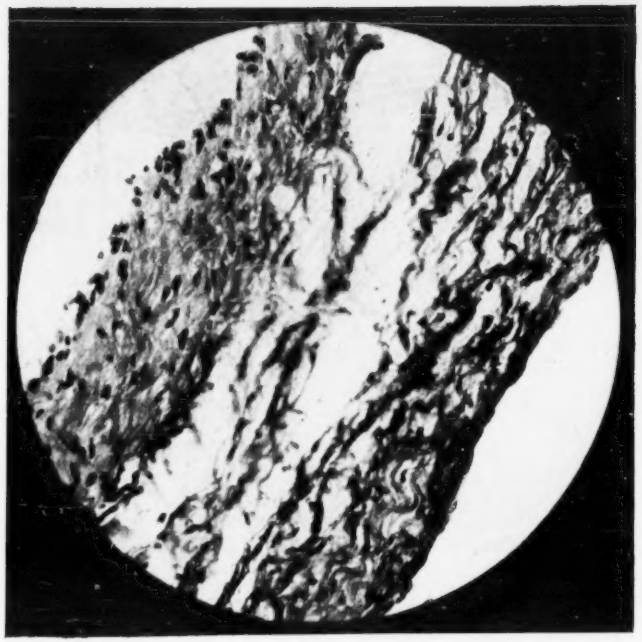


FIG. 4 (top left).—Photomicrograph of inner layer of diverticulum, showing the sheet of collagenous fibrous tissue, on left side lined by mesothelium, and on right side with an attached tag of cerebral tissue. (Hæmatoxylin and eosin × 250.)

FIG. 5 (top right).—Photomicrograph of outer layer of diverticulum, showing sheet of loose collagenous fibrous tissue, lined on both sides by mesothelial cells. (Hæmatoxylin and eosin × 250.)

FIG. 6 (lower left).—Postoperative encephalographs, showing air loculating in diverticulum before passing into lateral ventricles. The air within the diverticulum is outlined by dots.

DIVERTICULUM OF THE LATERAL VENTRICLE EXTENDING INTO THE POSTERIOR CRANIAL FOSSA: REPORT OF A CASE SUCCESSFULLY RELIEVED BY OPERATION

BY

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(RECEIVED 25TH NOVEMBER, 1946)

OBSTRUCTIVE hydrocephalus is on rare occasions complicated by the formation of a diverticulum from one or both lateral ventricles into the posterior cranial fossa. So far six cases have been reported (Penfield, 1929 ; Sweet, 1940 ; Childe and McNaughton, 1942 ; Peterson, 1942 ; each one case : and Pennybacker and Russell, 1943, two cases). Pennybacker and Russell, after performing ventriculography, recognized the condition pre-operatively in one of their cases, but in this, as in the remaining recorded instances, post-mortem examination provided most of the data.

Essentially, the condition is a pulsion diverticulum of the lateral ventricle through the medial wall of the trigone. It forces its way between the crus fornicis in front, and the fibres of the splenium above and behind, where they curve posteriorly as the forceps major into the occipital lobe. It then passes through the hiatus tentorii into the posterior fossa. The first stage in development is a localized thinning of the wall of the ventricle until only the pia remains. The pial wall is then ballooned outwards into the cisterna ambiens, and as it enlarges it comes into contact with the arachnoid mater of the cistern and thrusts the arachnoid before it. The pia remains intact, preventing communication between the ventricle and the subarachnoid space.

A diversity of terminology has been used in connexion with this condition. Sweet (1940) coined the term " ventriculostium " to connote a spontaneous, as distinct from a surgical, breach in the wall of the ventricle. This term, however, considers only the orifice and ignores the pia-arachnoid pouch which is an essential feature of the condition. Pennybacker and Russell (1943) emphasized the thinning and disruption of the brain substance, and accordingly employed the term " ventricular rupture." The pia, however, has not ruptured in any of the cases so far described, and, although the cerebral substance is thinned to obliteration, no communication develops between the ventricle and the surface cerebrospinal fluid pathways, as it should if the rupture of the ventricle were complete. Childe and McNaughton (1942) chose " ventricular diverticulum " as their descriptive term, and since a " diverticulum " is defined as " a pouch leading from a main cavity " (Dorland's Medical Dictionary) this word may be suitably applied. The ventricle shows localized pouching, and this terminology is not hindered by the fact that the wall of the pouch consists of only one tunic composed of pia, while the inner and middle tunics of the ventricle, consisting of ependyma and cerebral tissue respectively, are disrupted. Indeed, the ventricular pouch is analogous to those diverticula of the alimentary tract in which the muscular layer is deficient, the mucosal layer is in part ulcerated, and only the serosal coat is intact ; and which are still called diverticula in spite of these changes. " Ventricular diverticulum," therefore, appears to us to be the most easily understood and applicable term for the condition we are describing.

The primary hydrocephalic process which precedes the formation of a diverticulum may be due to an obstruction of the aqueduct or of the third ventricle. Diverticula have been observed in association with the following conditions :

1. Astrocytoma of the brain stem, deforming or occluding the iter, was present in Pennybacker and Russell's second case, in Sweet's case, and in Peterson's.
2. Benign gliotic stricture of the aqueduct was found in Pennybacker and Russell's first case, and is presumed to be the cause in our own.
3. Cholesteatoma of the third ventricle, with occlusion of the foramen of Munro, was present in Penfield's case.
4. Polar spongioblastoma of the hypothalamic region, filling the third ventricle and blocking the aqueductal orifice, was the primary pathological condition in Childe and McNaughton's case.

Childe and McNaughton (1942) consider that, in addition to the increase of pressure and consequent dilatation which occur in the lateral ventricles in these various pathological conditions, another factor is also necessary for the production of one of these diverticula. This is the absence of any large space-occupying lesion in the cerebellar region which might resist the entrance of the cyst through the hiatus tentorii. This latter feature probably accounts for the rarity of these protrusions into the posterior cranial fossa.

In most cases these diverticula are apparently symptomless. This doubtless explains why, in those cases in which a tumour has been the underlying cause and which have been submitted to operation, the surgical attack has usually been directed towards the tumour. Yet theoretically if the pial wall of the cyst were to rupture, either spontaneously or as a result of operation, a ventriculostomy would be produced which would short-circuit the obstructing lesion. However, Pennybacker and Russell's two cases are the only ones recorded in which the diverticulum has been approached at operation. A cerebellar exposure was used, and in both cases the diverticulum was incised and opened into the subdural space. Both cases, however, succumbed: one on the ninth postoperative day, following two Jacksonian epileptic attacks; and one shortly after operation, from an extradural hæmorrhage compressing the right cerebral hemisphere.

The present report concerns the successful surgical treatment of a diverticulum of the lateral ventricle by the establishment of a lateral ventriculostomy into the cisterna ambiens. It draws attention again to the fact that the wall of the diverticulum, as exposed surgically, consists of two layers, one of pia and one of arachnoid, between which is the collapsed subarachnoid space.

Case History

A man, aged twenty-three years, was referred by Dr. I. M. Allen of Wellington, and was admitted to this Unit on Sept. 14, 1945. He had been an apparently normal child until the age of five years, when daily frontal headaches had begun and had continued for ten years. At roughly three-monthly intervals he had suffered attacks of somnolence lasting for periods of two or three weeks, and in his seventh year these were diagnosed as encephalitis lethargica. When he left school, at the age of fifteen, he was three years below the normal attainment. He then developed attacks of vomiting associated with headache on waking each morning, and he also showed ataxia of the arms and reduced powers of concentration. Examination revealed low-grade papillœdema of both optic discs, and the radiographs of the skull showed increased convolutional markings. A cerebellar tumour was diagnosed, and the posterior fossa was explored by Mr. H. K. Corkill through a mid-line vertical incision. The reported positive findings were a thickening of the arachnoid mater and a dilatation of the cisterna magna. An operative diagnosis of arachnoiditis circumscripta cisternalis was made, and a cerebellar decompression was provided.

For the next seven years he was relieved of symptoms, and during that time he passed through his apprenticeship as a cabinet maker. Then, one year before his admission to hospital, he suffered a relapse with an initial two weeks' bout of projectile vomiting and neck stiffness. This was associated each day with violent frontal headaches which continued without remission. Co-ordination of his hands for writing and cigarette rolling decreased during the last six months. Finally his legs became ataxic and his speech dysarthric, and he was increasingly sleepy.

On admission he was found to be a heavy-looking youth with a large head (maximum circumference 59 cm.) and thin, hypotonic limbs. His alertness varied from sleepiness to mild euphoria. His recent memory and concentration were defective, but he made pungent criticisms of his medical examiners. He took eight minutes to subtract serial sevens from one hundred, making seven mistakes in the process, and he could only recall five digits in the digit-retention test. It is of interest that after his recovery he could not recall his admission to hospital nor his transfer by air ambulance. Examination disclosed bilateral papillœdema of 1 D without hæmorrhages. The right pupil was slightly larger than the left. There was no nystagmus. Slight weakness of movement of the right side of the face was detected. The limbs showed ataxia and hypotonia, more marked on the right than on the left side. Clonus was present in the right ankle, but the tendon jerks were not exaggerated; the plantar responses were flexor. He could not sit up unaided, and he walked with a pronounced zig-zag stagger. Lumbar puncture several weeks earlier had provided a clear cerebrospinal fluid (white cells, 10 per c.mm.; protein, 35 mg. per 100 ml.) under a pressure of 280 mm. of cerebrospinal fluid.

The provisional diagnosis, entertained on clinical grounds, was of mid-line cerebellar tumour which had lain latent for seven years under the influence of a decompression, but which had now expanded to the point of decompensation.

VENTRICULOGRAPHY.—On the day after admission ventriculography was carried out through bilateral parietal burr holes made under local anæsthesia. Both lateral ventricles were tapped at 3 cm. depth. The intraventricular pressure was found to be 150 mm. of cerebrospinal fluid. Air-filling of the ventricles was carried out from both sides, 300 ml. of cerebrospinal fluid being obtained. The six standard Lysholm projections were used in the *x*-ray examination (Figs. 1 and 2). Both lateral ventricles and the third ventricle were shown to be greatly dilated. The third ventricle filled well, but the upper end of the aqueduct filled only for 6 mm. and no air passed below that point. The appearances suggested a benign stricture of the aqueduct. A large air-containing cyst was observed behind the third ventricle and below the tentorium cerebelli. It measured 6·7 cm. wide, by 5·2 cm. high, by 4·9 cm. from before

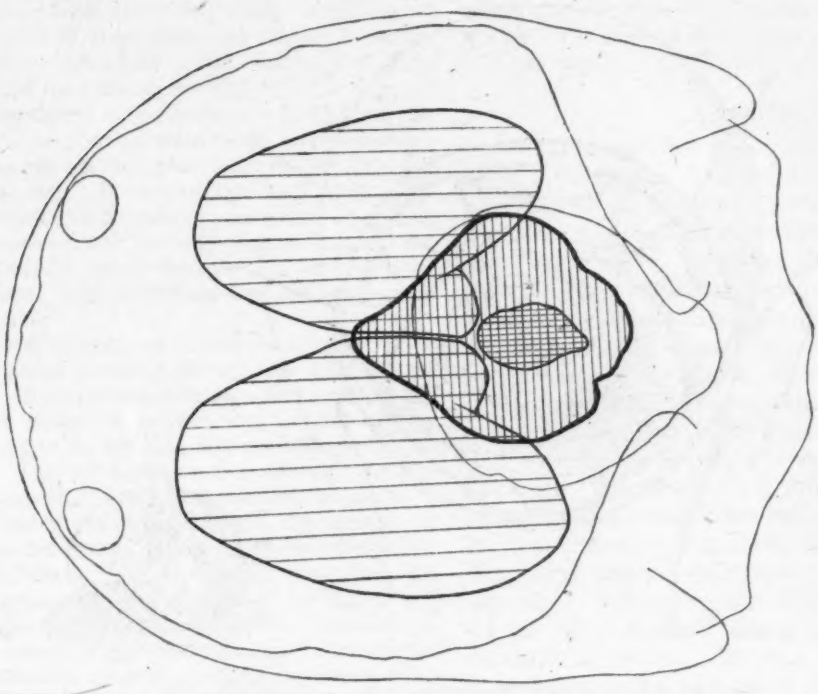

FIG. 2.—Tracing showing outlines of lateral ventricles, third ventricle, and diverticulum.

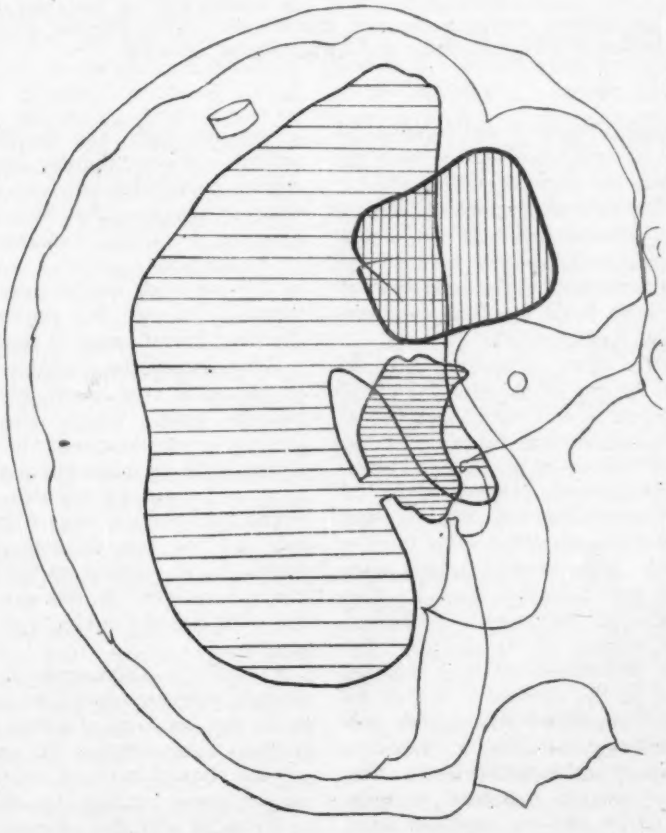

FIG. 1.—Composite tracing of ventriculograph, showing outlines of lateral ventricle (vertical lines widely spaced), third ventricle (vertical lines close together), and diverticulum (horizontal lines).

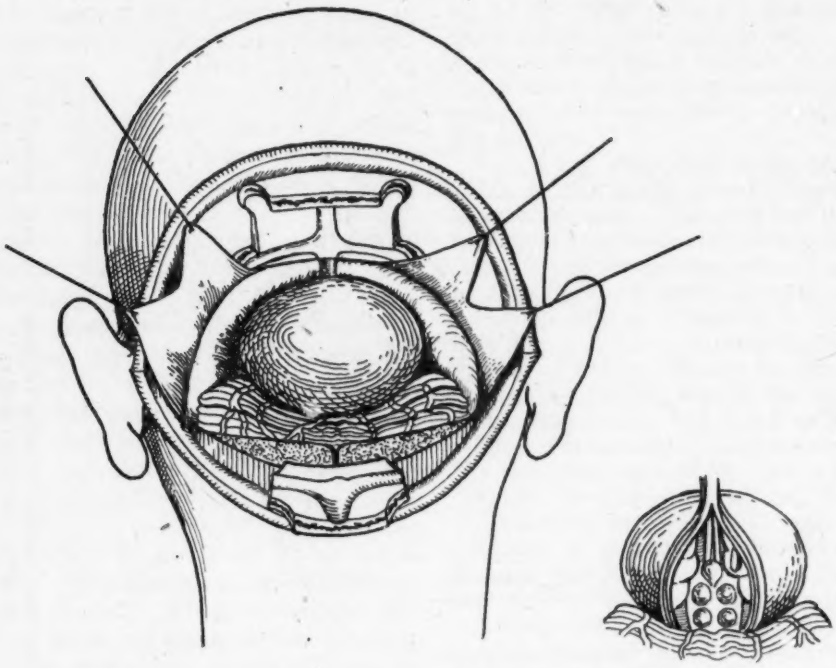

FIG. 3.—Sketch made after operation to show the position of the cyst between tentorium and cerebellum. (Insert: Structures revealed after opening of the cyst. Note the orifice in the medial wall of the right cerebral hemisphere, showing through the dilated hiatus tentorii above, and lateral to the pineal body and corpora quadrigemina.)

backwards. From the lateral aspect it was rhomboidal (Fig. 1). In the oblique postero-anterior projection the cyst was pear-shaped with the base inferiorly (Fig. 2). Integration of all views into three dimensions indicated a tent-like structure, with a concave floor and with a projection of the roof upwards and forwards between the vestibules of the lateral ventricles. The appearances were recognized as similar to those reported for diverticula by Pennybacker and Russell (1943).

OPERATION.—Immediately after ventriculography an operation was performed by one of us (M.A.F.) under intratracheal nitrous oxide, ether, and oxygen anæsthesia. A curved transverse scalp incision was made just above the level of the superior curved line of the occipital bone. A small bone flap covering the torcula Herophili and the proximal 2 cm. of each lateral sinus was turned downwards with the suboccipital muscles attached to it. The original decompression was clearly not functioning, since a thin widespread film of new bone had formed. This bone was removed. Although the exposed cerebellum seemed full, no tumour showed on its surface. The upper right sector of the cerebellum was then explored with a brain needle, and in the process a puff of air escaped. Immediately the cerebellar hemispheres collapsed, and when they were then retracted downwards a bluish white cyst was exposed, and incised (Fig. 3). The cyst lay between the tentorium cerebelli posterosuperiorly, the veins of Galen and the occipital lobes antero-superiorly, and the vermis and cerebellar hemispheres inferiorly; the pineal body, corpora quadrigemina, and mesencephalon bordered it anteriorly. It protruded upward through the dilated hiatus tentorii, which measured 3 cm. by 2·5 cm. exclusive of the portion taken up by the brain stem, to a vertical opening, 1·2 cm. high by 0·5 cm. wide, in the medial wall of the right hemisphere. Through this opening it communicated with the right lateral ventricle (inset, Fig. 3).

When incised the posterior wall of the cyst was found to consist of two closely apposed layers of thin membranous tissue, which were readily separated. The inner layer was attached to the margins of the ventricular stoma, while the outer was continuous with the arachnoid mater of the cisterna ambiens. The inner layer was then stripped off and cut away from the outer layer on either side, in the lateral angle between cerebellum and tentorium, so opening up the subarachnoid space of the cisterna ambiens. In this way a communication between the right lateral ventricle and the cisterna ambiens was attempted.

PATHOLOGY.—Specimens of both layers of the diverticulum were examined histologically. The inner membrane was made up of a thin wavy sheet of collagenous fibrous tissue between 70 and 80 μ wide. Its inner surface showed no well-defined boundary to the connective tissue, but had tags of cerebral white matter, up to 80 by 30 μ in size, adherent to it (Fig. 4, p. 100). Its

outer surface was lined with mesothelium composed of one or two layers of large cells with slightly flattened nuclei and scanty cytoplasm. These mesothelial cells presumably faced the subarachnoid space. The appearances of this membrane were consistent with its being pia mater to which portions of brain tissue were adherent.

The outer membrane was three times thicker than the inner (Fig. 5, p. 100). It was lined on both surfaces by flattened mesothelial cells similar to those seen on the pia externally. Between the two mesothelial layers were fasciculi of fibrous tissue interspersed with isolated mesodermal cells. This membrane had the appearance of arachnoid mater.

POSTOPERATIVE COURSE.—Convalescence was at first stormy, and patient remained drowsy and disorientated for five days. Respirations were slow and periodic for four days. A coarse nystagmus was present on the patient's looking to the left side, but not when he looked to the right. The left limbs were temporarily weaker than before operation, and the ataxia was increased in all limbs. Lumbar puncture pressures rose as high as 450 mm. of cerebrospinal fluid during the first four days. By the end of one month he had recovered from the ataxia, the texture of his voice had become lighter and less slurred, and his mental processes were more alert.

Tests for patency of the ventriculostomy were carried out two months after operation. Neutral phenolsulphonephthalein (2 ml. of 6 per cent. solution) was injected into the right lateral ventricle. After thirty minutes a lumbar puncture was performed with the patient sitting, and as the cerebrospinal fluid dripped away it was replaced by air. The dye did not appear until 60 ml. of fluid had been withdrawn. Radiographs taken during the procedure showed that the air loculated under the tentorium cerebelli in a space above the cerebellum formerly occupied by the diverticulum, and then passed into the right lateral ventricle and thence to the left (Fig. 6, p. 100). Some air entered the fourth ventricle, but none was detected in the third ventricle. It therefore appeared that the stoma between the lateral ventricle and the cisterna ambiens was patent and functioning. Incidentally the fourth ventricle was in its normal situation, and a correlation of this finding with the outlines of the third ventricle seen in the original ventriculograms, when only the upper end of the aqueduct filled, affords strong corroborative evidence of a gliotic stricture of the aqueduct.

The patient returned home ten weeks after operation. He felt fit, wrote and walked well, and was free of headaches. There was a residual trace of papillœdema, and a flicker of nystagmus. His mental age when tested by Raven's matrices was nine years, his intelligence quotient being 75 (Binet scale).

FOLLOW UP.—He was last seen at the end of a year. Throughout that time he had remained free from symptoms of raised intracranial pressure, and had performed odd jobs, helping his father in his workshop. It took some time to restore his confidence, and it was not until eleven months after operation that he returned to his former occupation of cabinet maker. He then appeared to be progressing satisfactorily. Examination showed normal visual acuity and no papillœdema or nystagmus, but there was slight ataxia of the left arm and left leg. His intelligence quotient as tested by the Raven matrices was 78 (Binet scale).

Discussion

Several noteworthy points arise from observations made in this case. The first is that diverticula may be expected in certain cases of advanced hydrocephalus, and can be detected preoperatively only by ventriculography. This reinforces the argument for routine ventriculography before craniotomy in all but the most clear-cut intracranial problems. In the earlier reported cases the ventriculographic appearances were often misinterpreted. Penfield (1929) diagnosed a supratentorial pouch; Childe and McNaughton (1942) regarded the shadow as that of the fourth ventricle displaced upwards by tumour; Peterson (1942) considered it to be a cystic tumour; and Pennybacker and Russell (1943) in their first case considered the appearance to be that of a dilated suprapineal recess of the third ventricle. Subsequently in their second case Pennybacker and Russell interpreted the diverticular shadow correctly. If the existence of these diverticula be kept in mind, the ventriculographic diagnosis is straightforward. Typically, the shadow in the lateral view lies level with the dorsum sellæ, and behind the posterior end of the third ventricle. It is separated from the dorsum sellæ by the thickness of the mid-brain. In the postero-anterior view the diverticulum is superimposed on the third ventricle and extends upward between the lateral ventricles.

The second point is that the cyst is composed of two layers, one of pia and one of arachnoid, between which lies the collapsed subarachnoid space. Sweet (1940), Childe and McNaughton (1942), and Pennybacker and Russell (1943) all noted this but did not emphasize its operative importance. We believe that merely incising the fundus of the diverticulum during the course of a cerebellar approach, and so opening the diverticulum into the subdural space, is not sufficient to provide a functioning ventriculostomy, as the two membranes comprising the diverticulum may remain in contact. The essential part of the operation is the separation of the inner pial membrane from the arachnoid, especially in the angles between cerebellum and tentorium close to the mid-brain, thus opening up the cisterna ambiens. In our patient postoperative tests with dye and encephalography demonstrated clearly that a lateral ventriculostomy produced in this way can function efficiently.

The operation of lateral ventriculostomy, as performed in our patient, has probably two factors which favour its success. One of these, the short-circuiting of the flow of cerebrospinal fluid, has just

been considered. The other, the provision of a cerebellar decompression, may of itself be adequate in a proportion of cases. We have had experience of a case of benign gliotic stricture of the aqueduct, proven at autopsy, in which symptoms had been relieved for ten years by a cerebellar decompression. The mechanism by which this relief was brought about is difficult to understand, but other surgeons (Pennybacker, 1940) have had similar experiences.

The favourable outcome of lateral ventriculostomy in our patient suggests to us that this is the operative procedure of choice when a diverticulum of this type is disclosed by ventriculography. In cases where neoplasm has been the cause, the neoplasm has always been deep-seated, and the operative attack upon it has so far always failed. A combination of cerebellar decompression and lateral ventriculostomy, followed later by deep *x*-ray therapy, might have benefited some of the recorded cases, at least temporarily. Pennybacker and Russell have advised that when gliotic stricture of the aqueduct is the cause, an anterior third ventriculostomy should be tried in the first instance. This latter procedure, however, fails to function successfully in an appreciable proportion of cases, and, moreover, it is not accompanied by the added benefit of a cerebellar decompression.

Summary

1. A case of presumed gliotic stricture of the aqueduct, associated with resulting hydrocephalus and the formation of a diverticulum of the right lateral ventricle, is described. The diverticulum presented between the tentorium above and the cerebellum below, and was visualized by ventriculography.

2. At operation the diverticulum was found to be lined by two layers, one of pia mater and one of arachnoid mater. A communication between the lateral ventricle and the cisterna ambiens was established by separating the two layers and removing the inner layer.

3. Importance is attached to the two layers of the cyst and to the effectiveness of the lateral ventriculostomy resulting from their separation. It is likely that the cerebellar decompression performed during this operation is also of therapeutic value.

We wish to thank Dr. E. D'Ath for advice on biopsy specimens, Dr. A. C. Begg for the ventriculographs, and Mr. H. K. Corkill, F.R.C.S., for his notes on the first cerebellar exploration.

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For Figs. 4, 5, *and* 6 *of this article see page* 100

A CASE OF MUSICOGENIC EPILEPSY

BY

DAVID SHAW

Sutton Emergency Hospital

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(RECEIVED 13TH DECEMBER, 1946)

DEFINITE and unequivocal examples of musicogenic epilepsy (epilepsy induced by musical sounds) are clinical rarities. In the most comprehensive review, Macdonald Critchley (1937) described eleven cases personally known to him and referred to a further nine culled from the literature. Some of the latter were by no means established, since only short anecdotal accounts were given of them. The onset of symptoms was noted as occurring later than is usual in idiopathic epilepsy. Further, many of the patients displayed an unusual knowledge and a keen appreciation of classical music. The musical stimulus might be of a specific kind, but the nature of the epileptic phenomena varied considerably; in some only minor attacks were induced, and in others only major attacks. The importance of the emotional state was stressed by Critchley, particularly in the period between first hearing the music and the onset of the attack. Speculations about the pathogenesis of this unusual form of epilepsy were made. It was accepted from the evidence and description of these cases that hysteria is no explanation, and an opinion was expressed that a conditioned reflex to certain musical sounds may be present. Critchley in 1942 briefly reported two further cases. In one an emotional disturbance set up by classical music was closely related to the actual seizure, and in the second it was only certain notes or tones that induced an epileptiform fit. In this latter case there was a history of closed head injury nine years previously. Taylor (1942) reported a further case, in which a head injury occurred six years before the occurrence of occasional epileptiform attacks. These attacks bore a close relation to music, and finally both major and minor attacks were readily induced by it.

Case Report

The patient, a married woman of 44, of German origin, came to this country when Hitler's succession to power in 1932 seemed imminent. She comes of a middle-class family in Saxony. Her sister is reported to have died of "fits" as a child. The patient developed normally and did very well at school, which she left at the age of 15. She then did clerical work, and later became a secretary to a large German Film Company and travelled widely. She was cosmopolitan in outlook, and politically strongly democratic and hence bitterly opposed to the rapidly growing Nazi philosophy. In England she worked regularly as a secretary until just after the outbreak of the war. In 1935 she had a liaison with a married man, who died suddenly, and after she heard the news she had an amnesic and confused episode lasting several hours, during which she wandered aimlessly around the streets. She married some four years ago, her husband serving for much of this time in the Army overseas. She is happy with her husband, who is very considerate and sympathetic. Her menses are normal and regular. She had an appendicectomy eleven years ago. There is no history of any convulsions in early life, but she had a nervous breakdown in 1929. At this time she was depressed, but recovered after a rest in the country. There is no history of head injury. She is ordinarily vivacious and energetic, prides herself on her efficiency, and is sociable and very popular, artistic, and sensitive to "atmosphere." She seeks her own way and is rather argumentative. She is very keen on good music, which at any time will move her very much, and is herself a moderately good pianist.

In February, 1941, she had a period of automatism while speaking on the telephone. She had no recollection of events during the attack and, in fact, put through the call again five or ten minutes later and repeated her message. Similar momentary "blank attacks" recurred on the average of one every two or three weeks. They occurred at any time, although much more frequently during the day. On two or three occasions she was

incontinent of urine. Her memory, previously very good, became unreliable; embarrassing mistakes and difficulties in connexion with her secretarial work occurred, and she herself gave up the job. The "blanks" continued. She became depressed, sleepless, and worried by the situation in which she found herself. She was treated with small doses of phenobarbitone and psychotherapy, but with no relief to her symptoms. She obtained night work as a packer in a food factory, since her "blanks" were much less frequent at night. In a communication to her friend and subsequent employer, she complained at this time about her bad memory and grumbled about the incessant radio programmes at the factory where she worked. In April, 1943, she was sent for a period of convalescence at the Lady Chichester Hospital, Hove. There the connexion with music first became apparent. A typical attack occurred when she was in the hospital Chapel listening to the organ. Dr. F. Reitman observed that music induced "a dreamy state lasting about five minutes, followed by a severe generalized headache." Two major attacks were induced by music. They commenced with conjugate deviation of the eyes and a turning of the body to the right; tonic and clonic phases followed, and, after a brief period of unconsciousness, a transient confused state. Corneal reflexes were present but bilateral extensor responses were noted.

At this time the EEG was done on two occasions by Dr. Cobb at Haywards Heath E.M.S. Hospital. On the first occasion the report was as follows:

> "*Resting:* Low voltage record consisting of about equal proportions of 2 rhythms—11 c/sec. and about 20 c/sec. up to 25 microvolts. In addition there are many slower waves, single and in short bursts at about 6 c/sec. of about the same voltage. *On overbreathing* (3 minutes) there is a slight increase in the number and amplitude of the slow waves, persisting for some time."

Sedatives were discontinued and she "enjoyed" music, and after fourteen days a major attack occurred. A second EEG was done and reported on as follows:

> "Dominant rhythm at 12 c/sec., rather irregular and not very persistent, voltage up to 50 microvolts and blocked by eye opening. There were other rhythms present. (1) Continuous 20 c/sec. rhythm, mostly of low voltage, but occasionally comparable with that of dominant rhythm. (2) Much 4–6 c/sec. at about same amplitude as dominant rhythm. (3) One short burst of high voltage 3 c/sec. waves. *On overbreathing* (3 minutes) there was a great increase in slow activity persisting for a considerable time and including several short bursts of high voltage 3 c/sec. wave and spike complexes."

The conclusion was that the response to overbreathing was now quite typically epileptic.

She was transferred to Sutton E.M.S. Hospital for further investigation in August, 1943, coming under the care of one of us (D.S.). Physical examination showed her to be a well-nourished, heavily-built woman. Blood pressure was 110/70 mm./Hg. No significant abnormality was elicited in the central nervous or other systems. Cerebrospinal fluid pressure was 240 mm. C.S.F. and the Queckenstedt test was qualitatively normal. The Wassermann reaction was negative in blood and cerebrospinal fluid. A radiograph of the skull showed no abnormality. During an EEG examination gramophone records were played (a Tosca aria and a noisy jazz record). The patient became tearful and emotional, but no attack was induced, nor was any change noted in her EEG. Two brief petit-mal attacks were observed while she was in hospital. They were not related to music. She left hospital after a month and continued to attend the Maudsley Hospital as an out patient. She managed to carry on in a secretarial job as an employee of a former acquaintance and fellow-countryman, but both minor and major turns persisted and were now becoming more easily "fired off" by musical stimuli. They occurred by day and by night, and in the case of the latter were often connected with a dream about music. Life was now becoming very difficult for the patient. She avoided music, as she said, "like the plague," and the situation had reached absurd lengths. If they went out together her husband would make a preliminary reconnaissance to find a café without a wireless or gramophone, and even the street musicians near her place of work were bribed by her employer to keep away from the vicinity. She had been treated during this period as an out patient with Caps. "epanutin," gr. 1½ b.d. and later t.d.s., and Tab. phenobarbitone, gr. 1 daily, without any demonstrable effect on the frequency of the seizures. During this period she put on nearly 3 stone in weight, reaching 15 stone, and was treated with Tab. thyroideum siccum gr. 1½ b.d.

She was readmitted to Sutton E.M.S. Hospital on Jan. 28, 1946. She was now voluble and rather more tearful and emotionally unstable than formerly. Always co-operative, she would nevertheless quickly get put out and become irritable. She demanded that all allowances be made for her susceptibility to music. There was no evidence of a general intellectual deterioration, but tests showed an impairment of retentive memory. She was intensely self-centred. Firstly she worried over her failing memory and the consequent difficulties at work, and secondly, her German origin—which she did her best to hide—was a source of considerable distress to her. She was afraid of being considered a Nazi sympathizer in view of her Aryan descent. On the other hand, she expressed fears that Nazi organizations in London would force her to join their ranks under the threat of harming her relatives in Germany. The fate of her parents was causing her considerable anxiety. During the height of the 1940–1941 blitz on London she had been at first fortified by music. She had made a practice of putting on her radio as loud as possible to drown the noise of the air-raids. But it now seemed to her that music was "distorted" in some way and invariably induced unpleasant emotions.

Minor attacks were now almost invariably induced by music. In these she suddenly felt "dead," and regained consciousness feeling drowsy and muddled for about half-an-hour. These attacks were frequently followed by a period of automatism lasting from twenty minutes to an hour, and in these episodes, of which she had no

FIG. 1.—Continuous EEG record from the left parietocentral region during musicogenic fit. Rhythmical potentials appear 5 seconds after the cessation of respiration with onset of tonic spasm. The record shows the progressive increase of amplitude and decline of frequency of the potentials as the fit proceeds (see text).

recollection, she was reported to have pulled back the blackout curtains on one occasion, and on another to have wandered off from her office in a dazed state. She stated she had even done some shopping or eaten her meal in her usual café with no memory at all of having done so. Characteristically, there was no warning of the attacks, which averaged three or four a month.

The major attacks occurred less frequently, one in every two or three months, and were also usually induced by music, but not invariably. They occurred both by night and by day, without aura. She had bitten her tongue and micturated during the attacks on several occasions.

Again no significant abnormality in the central nervous system was elicited on clinical examination, but the blood pressure was now 160/110 mm./Hg. The urine was normal. On lumbar puncture the cerebrospinal fluid pressure was 200 mm. C.S.F., and the C.S.F. was qualitatively normal. Radiographs of the skull showed no bony abnormality, and when further radiographs were taken following air replacement by the cisternal route by Mr. McKissock, no distortion of the ventricular system was found. Later, following the injection of an opaque substance into both carotid arteries, *x*-ray pictures of the head revealed a normal vascular appearance. Aural investigations by Miss E. Whetnall revealed no abnormality in the ears. The hearing tested by the audiogram was normal, and no subjective or objective response occurred to any tones except to 512 c/min., which, when varied in intensity and interrupted, was unpleasant to the patient. She became emotional but no fit ensued. She was similarly irritated by the Barany noise box. When the patient watched a revolving drum the direction of which was reversed, the optokinetic nystagmus obtained to the left side was greater than that obtained to the right. This finding suggested a central lesion on the left side.

Attacks Deliberately Induced by Music.—Throughout her stay in hospital no spontaneous seizures occurred, but attacks were successfully induced by music on each of the nine occasions attempted. Various kinds of music, from a musical comedy song to a Wagnerian Overture, have all produced varying degrees of emotional agitation and tearfulness followed by a fit. The pattern of the fit was repeated on subsequent occasions and the vesical incontinence occurred twice.

On hearing music she became agitated immediately, and talked rapidly, repeating various inconsequential comments in an effort apparently to distract her attention. She seemed to talk for the sake of talking. After ten minutes her right hand began to make pawing movements —which widened in range. Then head and shoulders flexed, and her right hand slowly went up to her nose which she gripped firmly. She stiffened in a tonic spasm, pursed her lips markedly, held her breath and became cyanotic, staring ahead with fixed congested eyes. This phase lasted altogether from two to three minutes. No abnormal neurological signs were elicited. She then got up from her chair, fumbled about in a confused way, muttering and evidently looking for her handbag. Contact was gradually re-established in spite of the continuing music. She complained of headache and asked repeatedly how she had managed to get into the room. There was no recollection for any of the conversation during the period just before the fit.

A series of electro-encephalographic investigations were carried out at the Maudsley Hospital. With the patient lying at rest, records were taken with a Grass 3 channel apparatus. Bipolar leads were used. The alpha rhythm was of low voltage, irregular in form and varied in frequency from 10–13 c/sec.; the distribution was symmetrical, the rhythm being seen best in the lower part of the hemispheres with antero-posteriorly placed bipolar leads, but better still with transverse electrode positions. Blocking to visual stimuli was normal. Continuous medium voltage fast activity at 20–22 c/sec. was seen in the fronto-central regions. With all transverse electrode placements irregular moderate voltage (50–70 μv.) bilaterally synchronous rhythmic potentials were seen. Among these, three rhythms could be identified having slightly different amplitudes, viz., (1) 3 c/sec. at 60–70 μv.—irregular complex wave forms in bursts of 2–3 waves, coming chiefly from the post central areas, (2) 5–6 c/sec. potentials at 40–50 μv. having relatively sinusoidal appearance in the lower central areas (theta rhythm), and (3) 4 c/sec. potentials at 50–60 μv. rather irregular in form, tending to lateralize to the left side in the anterior temporal region. No focal location for the potentials of this discharge could, however, be obtained with any constancy.

The EEG was then recorded while music was played. No significant change in the rhythms was seen before the onset of the fit. During this phase, which lasted from three to five minutes, signs of emotion, however, were evident. The onset of the fit on each of four occasions was heralded by an abrupt cessation of respiration, coincident with tonic, generalized muscular contraction which was evident in the EEG record as fast irregular activity, conducted probably from neck muscles. The muscle contraction was not sufficient to result in significant change of posture, although slight flexion of the head and trunk was evident on one occasion. During the initial few seconds automatic rotatory movements of the right arm were noticed, with pouting of the pursed lips. Six to eight seconds after the cessation of breathing, low voltage (30–40 μv.) 6–7 c/sec. potentials appeared synchronously and with equal amplitude on the two hemispheres. During the succeeding 72–112 seconds, until respiration recommenced, the potentials showed a steadily progressive increase of amplitude, with progressive decline in frequency, and finally developed a rhythmical high voltage (150 μv.) 2½–3 c/sec. bilaterally synchronous discharge. When respiration was re-established, this discharge lost its rhythmical sinusoidal appearance, the waves becoming irregular in outline, slower (1–2 c/sec.), and of lower voltage (Fig. 1). A gradual return to consciousness was now evident, the patient behaving in a dazed manner for which there was subsequent amnesia. This period lasted variously from ten to twenty minutes.

While music was played the patient showed overt signs of emotion. Fig. 2 is a record of the respiratory excursions, recorded on the drum of a Sandborn B.M.R. apparatus from which the lime had been removed. Fig. 3 demonstrates the changes of heart rate during the

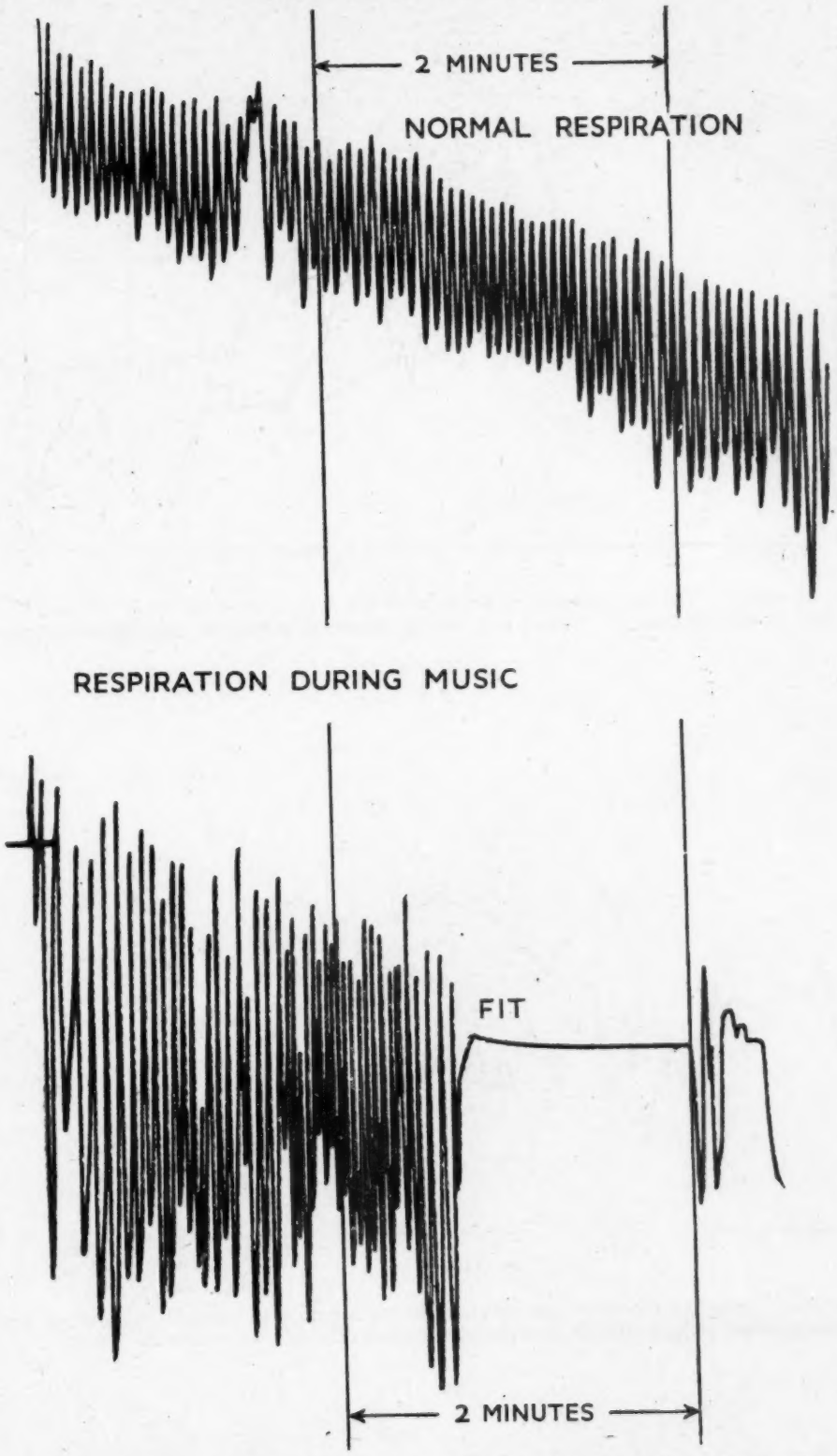

FIG. 2.—Record of the respiratory excursions recorded on the drum of a Sandborn B.M.R. apparatus from which the lime had been removed.

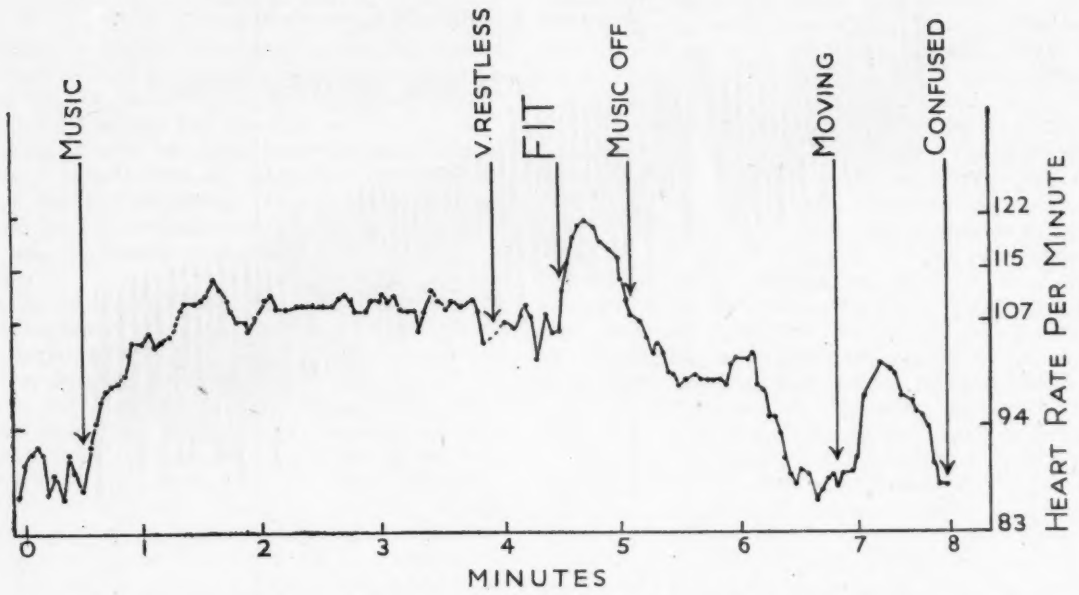

FIG. 3.—Shows changes in heart rate during the pre-fit period of musical stimulation.

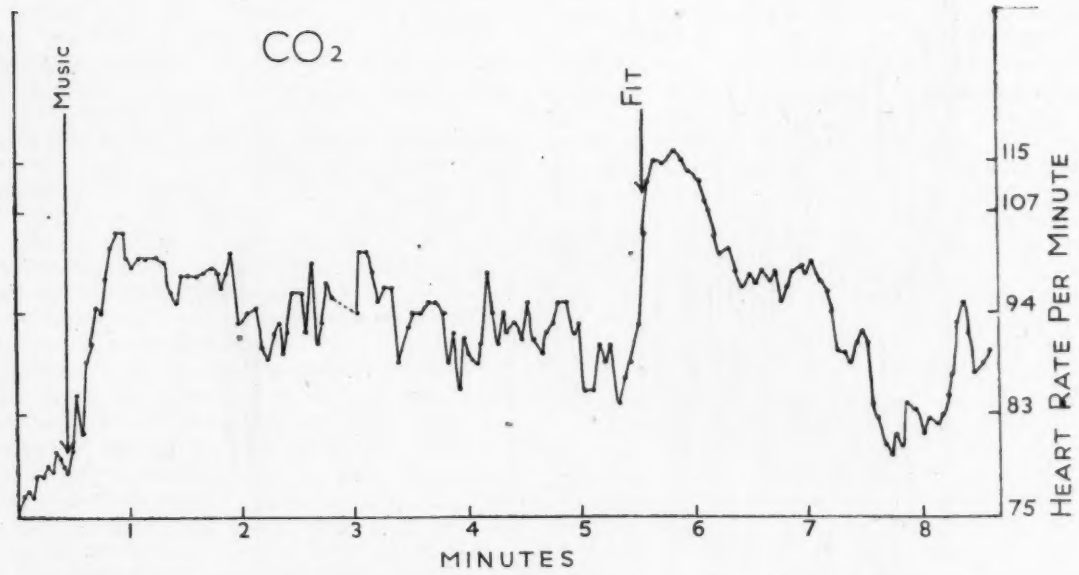

FIG. 4.—Similar record of the heart rate changes during a period of musical stimulation, while the patient breathed oxygen containing 5 per cent. carbon dioxide.

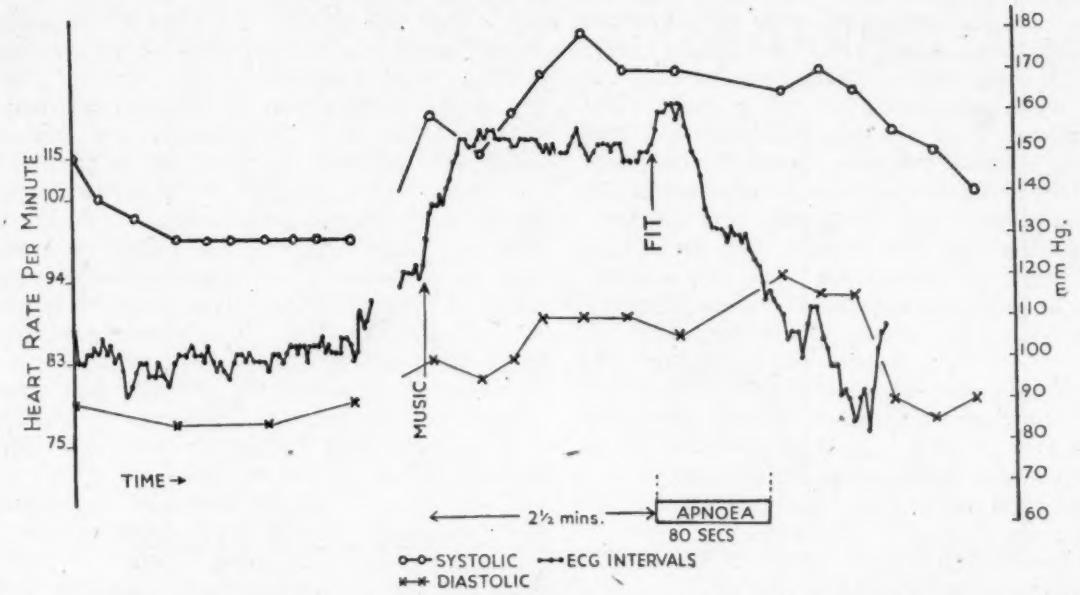

FIG. 5.—Composite record of the heart rate and blood-pressure changes (taken by sphygmomanometer from the arm) during a further investigation.

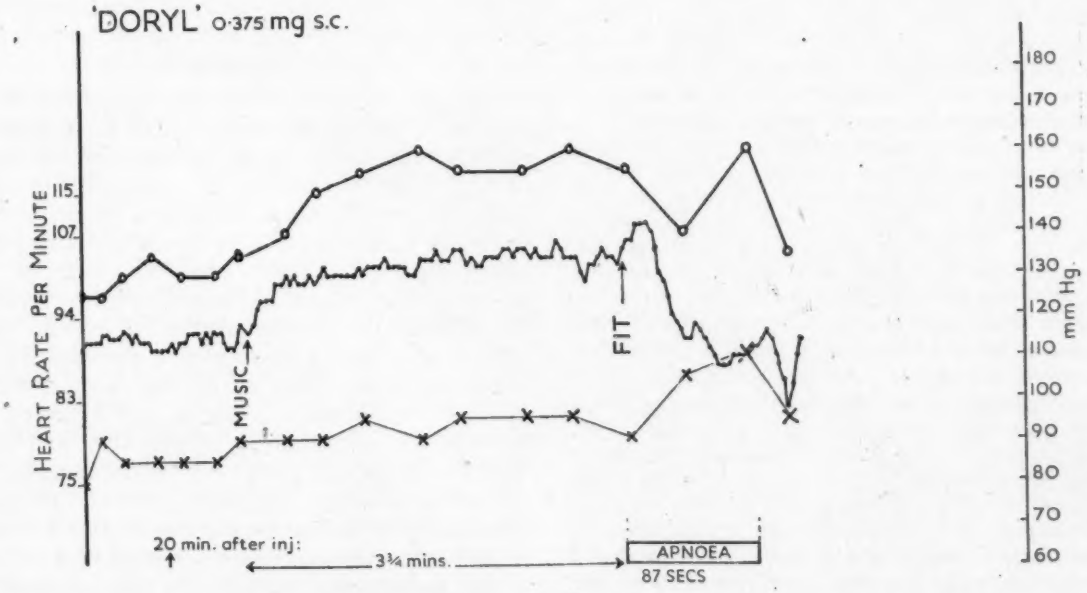

FIG. 6.—Heart rate and blood-pressure changes after injection of 1 c.cm. of " doryl " intravenously.

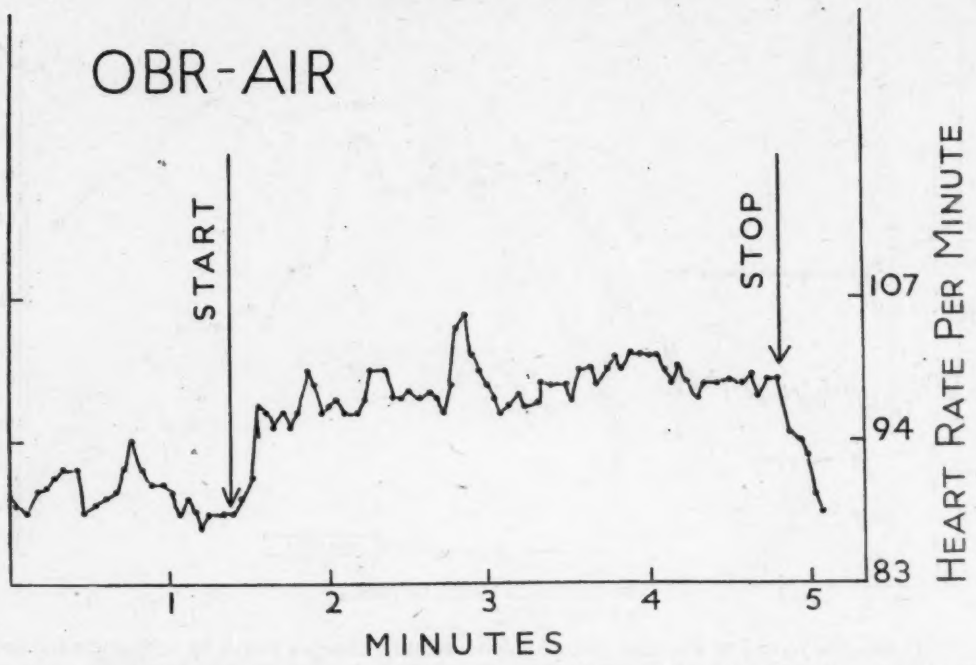

FIG. 7.—Record of the heart rate taken during a period of three minutes' voluntary overbreathing.

pre-fit period of musical stimulation. This was obtained by recording the arm-to-arm electrocardiogram on one channel of the Grass equipment (the other two channels recording the EEG). With a constant paper speed, variations in the distance between five successive R-waves of the electrocardiogram, measured in millimetres, give an accurate account of the heart rate. Fig. 4 is a similar record of the heart-rate changes during a period of music stimulation, while the patient breathed oxygen containing 5 per cent. carbon dioxide. Fig. 5 is a composite record of the heart-rate and blood-pressure changes (taken by sphygmomanometer from the arm) during a further investigation. Fig. 7 is a record of the heart rate taken during a period of three minutes' voluntary overbreathing. These investigations demonstrate increased depth and frequency of respiration, significant increase of heart rate, and a rise in systolic and diastolic blood pressure while music was played. A further increase of heart rate and blood pressure is observed at the onset of the fit. Fig. 4 illustrates that breathing 5 per cent. carbon dioxide facilitated the increase of heart rate and did not prevent the subsequent fit. In this case, therefore, the mechanism of fit precipitation was not alkalosis from overbreathing. It should also be recorded that voluntary overbreathing of much greater depth for three minutes had not induced a fit, nor equivalent increase of heart rate.

In view of the increased heart rate, blood pressure, and respiration rate during the playing of music, it was decided to observe the effects of a drug having an acetylcholine-like action. "Doryl," 1 c.cm., was injected intramuscularly and the procedure repeated. This did not prevent the development of a fit, but in the opinion of observers the objective signs of emotion were less evident while music was played. This observation gains some support from the heart rate and blood-pressure changes, both of which were less on this occasion (Fig. 6).

Discussion

It seems clear that we are dealing with a case of epilepsy. For the following reasons the suggestion that the musicogenic phenomena are a manifestation of hysteria can be disposed of, at any rate as far as this case is concerned. There is a family history of epilepsy. Urinary incontinence has occurred in the attacks on several occasions, and the fits observed have frequently been followed by a period of automatism. Major attacks have also been reliably witnessed and have been accompanied by tongue-biting and urinary incontinence. Further, the EEG examination made in 1943 showed the presence on overbreathing of the wave and spike complex discharge, and this would suggest an idiopathic ætiology. However, minor fits began at the age of 41 and at first bore no relation to music. As Critchley observed in his cases, the time of onset in this patient was later than is usual in cases of idiopathic epilepsy. Like the cases reported, full neurological investigations have failed to demonstrate a lesion in our patient. However, the evidence suggests a local onset for the fit in this case. In the deliberately induced fits it was repeatedly noticed that the movement first began in Jacksonian

fashion in the right hand and arm, with adversive turning of the head and eyes to the right. This suggests a focal epileptogenic area in the left hemisphere, probably the left temporal lobe. This is further supported by the results of the optokinetic test, and to a certain extent by the EEG. But of the nature of the focus we have no knowledge. The air studies and arteriogram were normal.

Psychological examination showed that, although superficially well adjusted, the patient was neurotic. There is an earlier history of a nervous breakdown induced by stress, and she has shown a tendency to react explosively to emotional stimuli; she became amnesic and confused after hearing of her lover's sudden death. Was this an earlier manifestation of epilepsy? In general, the musical stimulus is of a non-specific kind, although it is true that a pure tone of 512 c/min. when varied produced an emotional response, but no fit. Fits are induced by any kind of music, seemingly. The patient has always been keenly appreciative of music (perhaps over-emotional to it), and only latterly has found that musical sounds are distorted and produce an unpleasant emotional response. Critchley has discussed two different views of the pathogenesis of musicogenic epilepsy—the physiogenic and the psychogenic. In the first it is supposed that music itself induces the fit by causing increased cerebral blood flow. Records taken of the heart rate and blood pressure during the stimulation period and also throughout the fit show that there is a marked adrenaline-like response commencing immediately the stimulation is given and continuing throughout the initial stages of the seizure. It has also been suggested that the hearing of music might induce overbreathing and thus precipitate a fit by alkalosis in a latent epileptic. Records of respiration do indeed show overbreathing, and of the type commonly associated with emotion, that is, of greater depth and increased frequency, and with irregularity of both depth and frequency. However, voluntary overbreathing for three minutes produced less increase of the heart rate than when listening to music at rest, and no fit was ever produced by this procedure. Further, when the patient breathed 5 per cent. carbon dioxide while listening to music a fit supervened in the usual way. The possibility that alkalosis from overbreathing is the cause of the fit in this case can, therefore, be excluded.

The heart rate and blood-pressure changes are of particular interest in a case of musicogenic epilepsy because of the association of such changes with audiogenic fits in rats (Lindsley and others, 1942). The signs of emotion, restlessness, lacrimation, and overbreathing were invariably observed in this patient when she listened to music, and this association has been emphasized in other cases (Critchley, 1937). On the four occasions when records were made, similar heart rate and EEG changes were observed, indicating a temporal sequence of events. When the musical stimulus was given, and sometimes *during the brief anticipatory period preceding it*, a sharp rise in heart rate and systolic blood pressure occurred. After thirty or forty seconds the heart rate and blood pressure ceased to increase and remained steady, the normal variations of heart rate being less evident.

The type of EEG discharge during the fit is that commonly seen in epileptic psychomotor seizures (Gibbs and others, 1936; Jasper, 1941) and the initial frequency of the discharge, together with its bilaterally synchronous occurrence, is in favour of a basal origin for the cerebral dysfunction (Jasper, 1941; Cobb, 1944; Walter and Dovey, 1944). The progressive facilitation of the discharge indicates a focal origin, recruiting progressively more and more neurone groups.

It is relevant to consider the similarities and differences which this case shows with the audiogenic fits in rats investigated by many workers (Maier, 1939; Morgan and Morgan, 1939; Maier and Glaser, 1940; Lindsley and others, 1942). In certain strains of rats, though not carried as a simple mendelian dominant, a susceptibility to abnormal behaviour culminating in convulsions is found as a response to high-pitched sounds (whistle, key-jingling, etc.). The abnormal behaviour in response to sound stimuli shows two phases, bearing resemblance to the case reported here. In the first phase, seen as violent, undirected running and jumping ending in tonic-clonic convulsions, there are marked changes in heart rate and blood pressure, usually an adrenaline-like effect (Lindsley and others, 1942). The second phase is one of inactivity, the animal being comatose, showing no response to sensory stimulation. The reflexes and righting responses are absent and the animal can be moulded into various positions. There is a gradual return to normal. During this phase the heart rate falls sharply and then gradually returns to normal. Lindsley and others (1942) found that, if their rats were restrained, no fits occurred. In the unrestrained rats, the heart rate usually showed a sharp increase of rate of considerable magnitude and usually a decrease just before the attack. In other cases there was an initial fall in the heart rate. In our patient increase in the heart rate was invariable. The temporal sequence of events in the audiogenic

seizure is emphasized by these writers. This consists of (1) increase of heart rate, (2) a marked electrocortical discharge in the EEG at the onset of the attack. In the present case the EEG characters are clearly different from those in the rats, though it is doubtful whether the two may be compared. In the rat the discharge—slow waves and mixed spikes and waves—is maximal at the onset of the fit and does not show the progressive build-up evident in our patient.

Lindsley and others (1942) found that physical restraint prevented the occurrence of seizures in their rats. Partial curarization had a similar effect. Following vagotomy the seizures were also prevented and no heart-rate changes occurred to sound stimuli. Since in the present patient the heart rate and blood pressure preceding the fit invariably showed an adrenaline-like response, an attempt to balance this with a drug having an acetylcholine-like action was made. Doryl injected intramuscularly resulted in less heart rate and blood-pressure change to music, and the overt signs of emotion—as judged by observers—were less during the stimulation phase, but the fit was not prevented. If the result of this experiment is considered significant, it may be regarded as evidence that the peripheral or cerebral vascular effects of emotional over-activity are not of major importance in the production of fits in this patient.

The earlier workers on audiogenic seizures in rats had likened the phenomena to the " experimental neurosis." Maier (1939) induced fits by a conflict situation in which the rats were forced to respond to a physical stimulus which they had previously been conditioned to avoid. Maier and Glaser (1940) found that " barriers to response " to stimuli increased the frequency and susceptibility to fits. On the other hand, Lindsley and others (1942) prevented fits by restraining their rats. In the rats who were not restrained but who did not develop fits during auditory stimulation, some form of " substitute behaviour " was noticed, such as nose or ear rubbing and teeth chattering. It was observed that our patient would talk rapidly and become agitated when music was played. She would repeat various inconsequential comments in an effort apparently to distract her attention. However, she could not prevent the fit by these means. It has been noted already that Critchley (1937) considered the possibility that a conditioned reflex to musical sounds might have been created in these cases. In our patient's case, fits, both major and minor, had occurred before any relation to musical stimuli became apparent, and the evidence suggests that she is an idiopathic epileptic. The relationship to musical precipitation started during the London blitz, when no doubt emotional stress was associated with hearing music. After this the association with fit precipitation became progressively more complete. In the case of the rats, Lindsley and others (1942) conclude from their data that auditory stimulation rather than conflict neurotic reaction is the chief component in the production of seizures, and these workers suggest that the auditory stimulus excites autonomic centres in the diencephalon by direct spread. In the particular case reported here, there is much to suggest a conditioned process. Such a conditioned reflex cannot, however, be explained as a simple pattern involving the acoustic nuclei and the diencephalon. Masserman (1943) in an extensive review of his own and others' experiments, concludes that the hypothalamus behaves not as an afferent experience-mediating organ, but as a way-station on efferent sympathetic and motor pathways, which cannot be conditioned by direct stimulation (Gantt, 1937 ; Gantt and Loucks, 1938). Attempts to condition " hypothalamic responses " to sound stimuli in lightly etherized animals failed, and such attempts left no change in the action potentials from the hypothalamus. The establishment of a conditioned response is dependent upon the " meaning " value of the stimulus, and from this it may be inferred that the function of the cerebral cortex is involved. This is supported by the fact that no fits could be produced by exposing the patient to pure tones, although she showed signs of emotion with 512. The dependence on harmonic sounds would suggest a cortical receptor level and the difference between " music " and pure tones for experience is one largely of " meaning." The fit pattern, the optokinetic responses, and the resting EEG pattern all suggest an epileptogenic zone in the left temporal lobe. The fits bear resemblance to the " dreamy states " seen in the temporal lobe epilepsy. However Beach and Weaver (1943) found that in the rat an intact cortex is not essential to the production of the fits. In fact, almost complete decortication increased the susceptibility to fits and the intensity and duration of them.

Although there are similarities in the temporal course of events between the epilepsy of this patient and the characteristic audiogenic seizures of rats, it would be unsafe to argue from the case of the latter as to site of origin of the epileptic discharge in the human. Against the clinical evidence indicating a focal discharge arising in the left temporal cortex is the evidence that no new pattern was observed in the EEG until six or eight seconds

after the start of the fit, and the fact that when such changes appeared they were equal and synchronous on the two hemispheres. It is possible that the electrodes were placed too far away from the site of origin of the discharge, with the result that by the time it reached them the rhythm had developed bilateral synchrony. This is known to occur in temporal-lobe discharges (Jasper, 1941). On the other hand there is evidence (Walter and Dovey, 1944 ; Cobb, 1944) that rhythms with the frequency seen in their case, having bilateral synchrony, are found in lesions in the neighbourhood of the third ventricle. The extremely slow " build up " of the rhythms during the fit demonstrates that the discharge is progressing in the brain very slowly. It seems reasonable to suggest that the site of origin of the discharge in this patient is deep in the left temporal lobe, that it spreads predominantly towards the basal brain, and that it only involves the cortex at a later stage in the development of the fit.

Summary

1. The development of a specific musical stimulus to fit production is described in an epileptic woman.

2. Extensive clinical investigations failed to reveal an acquired cerebral lesion, although the fit pattern, optokinetic response, and inter-seizure EEG indicate an epileptogenic area in the left temporal lobe.

3. Increases of blood pressure, heart rate, and respiration while listening to music were observed in this patient. These were associated with overt signs of emotion.

4. Fits could not be induced by pure tones, although the patient felt emotional to a tone of 512, which persisted and was varied in loudness. Different kinds of music were invariably followed by a fit within five minutes.

5. Electroencephalographic studies showed a constant pattern for the development of the fit. No change of rhythm was seen while music was played before the fit began. The cortical discharge began six or seven seconds after the clinical onset. This discharge consisted of 6 c/sec. low voltage potentials having bilateral synchrony, steadily increasing in voltage and falling progressively in frequency to reach $2\frac{1}{2}$–3 c/sec.

6. The possible mechanisms of fit production are discussed.

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ELECTRICAL AIDS IN PROGNOSIS OF NERVE INJURIES

BY

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(RECEIVED 24TH AUGUST, 1947)

PERIPHERAL nerve injuries resulting from wounding with high velocity missiles may vary from complete disruption of nerve trunks to a mild stretching of nerves at a distance from the pathway of the projectile. When such stretching is sufficiently severe as to interrupt the individual nerve fibres, the resulting paralysis may be most difficult to distinguish from that resulting from anatomic severance of the nerve trunk, yet the prognosis and treatment are quite different. In our experience with 919 cases of nerve injury due to missile wounding there were four or five such "lesions in continuity" for every one with complete severance of the nerve. From our prolonged observation of patients with lesions in continuity, it was apparent that some of these lesions offered an insuperable obstacle to the progress of regenerating fibres, while many others spontaneously recovered a better degree of function than we could have hoped to confer by resection of the lesion and the most meticulous anastomosis.

Even when a lesion in continuity is exposed in the surgery it may be difficult to evaluate its chances for spontaneous regeneration. If electrical stimulation above the lesion results in contraction of muscles supplied by the nerve below the lesion, one may be confident that regeneration has taken place, but frequently the interval between wounding and surgical exposure of the lesion is too short to permit growing fibres to have reached the muscles which they supply.

Nerve Action Potential Studies

On the basis that regenerating nerve fibres should have established the property of conduction as they advanced toward the muscle, even before having achieved their goal, we endeavoured to pick up action potentials from the distal segment of the injured nerve while stimulating electrically proximal to the lesion. Berry and others (1944) had studied action potentials in the regenerating sciatic nerve of the cat after section and suture. They found the threshold of the regenerating fibres to be much higher, and their rate of conduction slower, than in the normal fibres, these factors approaching normal as the axonal calibre, studied histologically, increased with time.

We derived the stimulating current from a Model 3 Grass stimulator, passed through an electrostatically shielded transformer to minimize stimulus artefact, and delivered at the rate of 6 stimuli per second, diphasic spikes of from 0·05 to 0·2 milliseconds being used. Both stimulating and recording electrodes were of 24-gauge silver wire, each pair being embedded in a block of plastic material fashioned with a trough in which the nerve could rest and be insulated from the surrounding tissues. The stimulating electrodes were placed above the lesion, and the recording electrodes below. Action potentials were amplified, and visualized by a DuMont type 208-B cathode ray oscillograph. The sweep of the oscillograph was triggered by the same current which triggered the stimulator, permitting visualization of the stimulus artefact as well as the action potential. Photography was accomplished by the use of a reflex camera with a shutter speed of about 1/10 second.

In all cases in which muscular contraction was obtainable on stimulation with the Hinsey-Geohagan stimulator we were able to record action potentials from the nerve below the lesion. The type of record secured is illustrated in Fig. 1 (p. 99), which was taken at the time the ulnar nerve was transplanted at the elbow. The stimulating electrodes were placed just above the scarred portion of the

nerve, and the recording electrodes 11 cm. below. The diphasic action potential, 150 microvolts from peak to peak, followed the stimulus artefact by approximately 3 milliseconds.

Fig. 2 (p. 99) shows the 20-microvolt action potential recorded peripheral to a lesion of the sciatic nerve in the mid-thigh. In this case no muscular movement could be secured on electrical stimulation, so that the action current must have been due either to regenerating fibres which had not yet reached the muscle, or conceivably to surviving sensory fibres. The nerve was subsequently sectioned and sutured, and a few apparently intact fibres were visible in the cut ends. Unfortunately we have no cases in which action potentials were secured without the presence of muscular contraction on electrical stimulation, which have been followed to return of function without operative intervention. Thus we can only say of this method of investigation that it holds promise of clinical usefulness, but can present no concrete evidence of the extent to which it may be utilized at the present time.

Neuromuscular Excitability Studies

Another problem relating to regeneration on which the surgeon would like technical assistance is the question as to whether or not nerve fibres are growing across a suture line. After a nerve anastomosis has been performed it may be many months before growing fibres can reach the muscles and establish connexions adequate to make voluntary contractions possible. Any technical method which might shorten this interval of waiting for the demonstration of voluntary control should be of value to the surgeon. It has been well established that regenerating nerve fibres reach the muscle supplied a considerable period before overt motor power makes its appearance. It has been held that this time may be determined by the appearance of changes in the electrical excitability of the muscle which then take place. Should this be the case, valuable information regarding the prognosis might be secured at an appreciably earlier date than it could be ascertained by clinical examination alone. Many methods for determining this change in excitability have been advanced, each with its advocate.

Thus Moldaver (1942) is enthusiastic about chronaxie, while Bauwens (1944) believes chronaxie to be misleading, and prefers strength-duration curves. Ritchie (1944) and Marble and others (1942) use voltage-duration curves, and Pollock and others (1945) believe the galvanic tetanus ratio is valuable. In view of the wide divergence of opinion among different workers in the field as to the relative value of the various procedures, we felt it was impossible to decide which method would afford the most reliable information unless several prognostic tests were carried out simultaneously on each patient. Those procedures which we employed were rheobase and chronaxie, strength-duration curve, galvanic tetanus ratio, and relationship between anodal and cathodal closing contraction threshold.

To this end an apparatus was constructed that was capable of producing the stimuli required for these tests. It has been described fully elsewhere (Newman, 1946), and consists essentially of a source of square waves of current, the duration and intensity of which are subject to control by the operator. Polarity is capable of reversal, and the current through the tissues is independent of skin resistance.

The course of 33 traumatic nerve lesions, mostly resulting from bullet and shrapnel wounds, was followed to recovery of definite motor function. Of these cases twenty-four were subjected to nerve suture, the remaining nine recovering spontaneously. Eighteen of the lesions were of the ulnar nerve, ten of the median, four of the radial, two of the peroneal, and one of the tibial. In general, the muscle chosen for electrical testing was one as remote as possible from the site of wounding ; in the case of the ulnar nerve the abductor of the little finger was used as a routine, and for the median the opponens. By picking out one particular muscle, and following its electrical excitability from the initial examination until motor function returned, it was felt that a better comparison between the various methods of testing could be made than by testing all of the paralyzed muscles. An attempt was made to repeat the tests at intervals of not greater than two weeks, but furloughs and intercurrent operative procedures sometimes prevented this.

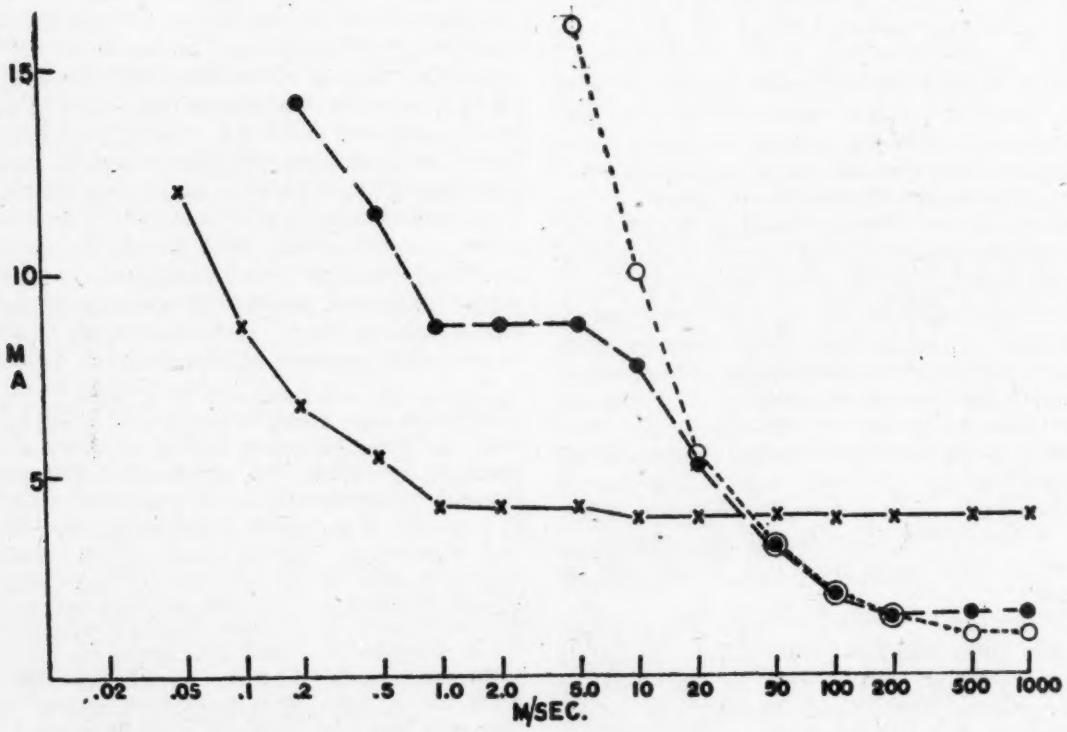
The testing was conducted in a warm room, the temperature never falling below 70° F. The indifferent electrode, a piece of cotton felt backed with lead sheet, about 10 by 10 cm., was moistened with saline and strapped to the extremity to be tested, above the lesion if possible. The stigmatic electrode was chamois covered, of an area of about 1 sq.cm. It was kept moist with saline, and applied to the point on the muscle which showed the maximum response to stimulation. Thereafter, this same point was employed in subsequent testing.

The threshold was first determined for stimuli of 1,000 milliseconds' duration, the stigmatic electrode being the cathode. Then successively shorter stimuli were used, and each threshold intensity recorded, until no muscular contraction was obtained with full output of 20 ma. The resulting values, plotted as intensity of stimulus against duration of stimulus, constitute the strength-duration curve. When the duration is plotted

on a logarithmic scale, curves are obtained such as are shown in the graph. Fig. 3 (p. 99) is an oscillographic record of the form of the stimulus obtained from the apparatus, which it will be noted is essentially square in conformation. Chronaxie was determined from the strength-duration curve by reading off the duration of stimulus at twice the rheobasic value by interpolation. The threshold intensity required to produce a single twitch at 1,500 milliseconds' duration of stimulus was next determined, and then the current was gradually increased until a contraction sustained throughout the entire time of passage of the current was obtained. This latter value divided by the former constitutes the galvanic tetanus ratio. In normal muscle this is about 4, while in denervated muscle it approaches 1. Polarity was then reversed, and the threshold for a single twitch with the anode as the stigmatic electrode recorded, to be compared with the threshold already obtained for cathodal closing contraction. The whole procedure took only a few minutes, and was well tolerated by the patients.

Analysis of the results obtained on repeated testing during the period of reinnervation demonstrated that all the tests employed showed a tendency in the majority of the cases to revert to the normal picture. Thus the extremely long values of chronaxie became shorter, and the reversed relationship between anodal and cathodal thresholds righted itself, while the rheobase tended to rise. However, in all the above-mentioned observations there was such a great variation in results from one examination to the next, with no abrupt change that could be depended upon as an indicator of reinnervation, that they were for all practical purposes useless in establishing prognosis.

Both the galvanic tetanus ratios and the strength-duration curves were, however, of real value in prognosis, as will be demonstrated by the following data. Of the cases followed to return of function, 54 per cent. showed a break, or discontinuity, in the strength-duration curve before motor power was re-established, the average time that the electrical change anticipated the clinical evidence of recovery being 97 days. Forty-eight per cent. of the cases showed a rise in the galvanic tetanus ratio to 3·0 or higher, which value we believe to be the lowest that can be used safely as a criterion of recovery, an average of 109 days before return of motor power. In 30 per cent. of the cases both tests showed a change before motor recovery, yet on the other hand 27 per cent. had established motor



Strength-duration curves obtained from the abductor of the little finger. The open circles show the initial reaction of the muscle, the closed or solid circles that prevailing during recovery, with a break in the mid-portion of the curve. The crosses show the curve obtained from the normal muscle of the opposite side.

function before any reliable evidence of electrical change was apparent. Thus it can be seen that with either one or the other of the two tests reliable signs of recovery were obtainable in about half the cases, while if both were employed this was raised to 73 per cent. Therefore, although in an appreciable percentage of the cases the tests failed completely to reveal the progress of reinnervation, in by far the majority they yielded information of considerable prognostic value.

Thus far only those cases which proceeded to motor recovery under observation have been considered. It is equally important to consider those in which we have electrical data but in which a lack of return of motor function might indicate failure of regeneration, in order to ascertain if the electrical tests may yield false evidence of recovery. In this connexion thirteen lesions, of which ten were ulnar, two median, and one radial, were followed for approximately one year without appearance of motor recovery. In four of these there was no electrical change to indicate regeneration, so these may be dismissed from further consideration. Of the remaining nine cases, two showed favourable electrical changes in both tests, five a rise in the galvanic tetanus ratio, and two a break in the strength-duration curve. In four of these cases the period of observation had been twice as long at least as the interval from time of suture to appearance of electrical changes, so that ultimate functional recovery seemed unlikely. It seems quite possible, however, that, although sufficient fibres had not regenerated to produce an active muscular contraction, a sufficient number had grown down to produce the electrical changes noted. In the remaining five cases the period of observation was not long enough to be sure that motor power might not yet appear. In only one case did electrical changes appear before theoretical considerations would permit of fibres reaching the muscle; this case must surely be considered a false positive sign from the electrical standpoint. However, it can be seen that in a not inconsiderable number of cases positive electrical signs of recovery were observed without actual return of useful motor function. This seriously detracts from the value of the tests in prognosis, where such evidence must be weighed in determining whether or not operative intervention is indicated, since such false positive findings would then result in undue postponement of operation. When it is considered that even the degree of reliability of results above detailed was secured only by dint of frequently repeated examinations, it is at once apparent that the results of isolated single examinations must be much less valuable, and should not be given undue weight.

Summary and Conclusions

An attempt was made to record, by means of amplifiers and a cathode ray oscillograph, nerve action potentials from injured nerves to determine the presence or absence of regeneration. Although the method showed promise of usefulness, sufficient data are not yet at hand to permit of a fair appraisal.

Determination of the galvanic tetanus ratio, and of the form of the strength-duration curve, is of practical value in establishing the presence of regeneration an appreciable time before clinical examination would be adequate for the purpose. However, neither are these signs always present, nor can they invariably be relied upon to establish the return of useful motor function. Since it is of the utmost importance in the proper handling of peripheral nerve injuries to determine at as early a date as possible whether or not regeneration is taking place, the electrical methods which we have described, as well as electromyograms and any other procedure which might reasonably shed light on this problem, are amply justified.

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ELECTROMYOGRAMS IN MUSCULAR DISORDERS

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(RECEIVED 18TH JULY, 1947)

Introduction

IN the routine work at this clinic during the last few years, electromyography has been found a reliable method for distinguishing between muscular dystrophies and lesions of the lower motor neurone. When other clinical methods have failed it has been possible by the aid of electromyography to differentiate not only between late distal forms of myopathy from peroneal muscular atrophy, but also proximal forms of muscular dystrophy from certain cases of proximal spinal muscular atrophy.

There are but few published observations on the electromyogram in cases of muscular dystrophy in which the modern technique introduced by Adrian and Bronk (1929) with coaxial needle electrodes has been applied. Buchthal and Clemmesen (1941 a) used this method in order to differentiate muscular dystrophy from neurogenic lesions. In genuine severe myopathy they found, as in the normal muscle, that voluntary contraction was accompanied by the interfering activity of many motor units. Only in extremely severe atrophy (observed in one muscle) did they note a slight decrease in the number of active units, as is seen in cases of mild injury of the lower motor neurone. In moderate or severe neurogenic lesions, on the other hand, the number of active units registered is markedly reduced. On maximal contraction, " single discharges " may be obtained without interference from neighbouring units, as had also been observed by Seyffarth (1938, 1940) and by Weddell and others (1944).

Bowden and Gutmann (1946) recorded the electrical activity of muscle in one case of progressive muscular dystrophy. Here, however, on maximal contraction merely a few action potentials were left, some of which were indistinguishable from action potentials characteristic of fibrillation.

The present paper is concerned mainly with a study of the changes in the electrical activity of voluntary muscle in man in various forms of myopathy. For the purpose of comparison, electromyographic changes in different types of lesions of the lower motor neurone are described.

Technique

Coaxial needle electrodes (platinum wire, 0·20 mm. in diameter, insulated by a glass capillary tube from a cannula of stainless steel with an outer diameter of 0·5 mm.) were employed. The action potentials were led off to a one-channel balanced condenser-coupled amplifier connected to one beam of a cathode-ray tube ; the other beam of the tube was connected to an oscillator which recorded the time in milliseconds or 1/100 second. The time constant was about 1/30 of a second, and the gain linear between 20–4,000 cycles per second.

For diagnostic purposes, it is sufficient to observe the picture on the screen. Only if the duration and size of the action potentials are to be exactly determined will measurements from tracings be necessary. In this study the picture on the screen was first observed at different sweep velocities. In order to obtain surveys of the course of the voluntary contraction, the sweep was then stopped and a picture was taken while the patient was making a minimal continuous contraction, slowly increasing to maximal. The speed at which the photographic paper was fed forward was 10 cm. per second.

In order to obtain detailed pictures of individual action potentials, the cathode ray tube was rotated 90 degrees, so that the sweep carried the ray horizontally over the screen about three times a second. When the film is running vertically in front of the tube, a series of such pictures one above the other is obtained. With the sweep velocity adopted, ½ to 1 cm. on the screen corresponded to a millisecond, which permits an exact determination of the duration and form of the action potentials.

Results

PRIMARY MUSCULAR DISORDERS

In the muscles under examination, the patient was asked to make a minimal contraction, slowly increasing in intensity, so that four or five different " units," recorded with the needle at the same position, could be followed from the start until they had merged into the activity of neighbouring " units." The position of the needle was then changed. In this way, at several positions in the muscle, samples of action potentials were available for quantitative determinations of both duration and amplitude. At the same time one could obtain an idea as to how many active units there were on maximal contraction.

The position of the needle is carefully tested under control of the picture on the screen. In large muscles it may often be difficult to separate the different " units." Sometimes, as found by Gilson and Mills (1941), one succeeds best with the point of the needle immediately under the fascia. The small intrinsic muscles of the hand and foot are the most easily examined.

The finding of a suitable position for the needle is largely a matter of chance. In the muscle there is a functional organization of different units, certain of them being activated by a slight contraction, others only as the contraction increases in intensity. The aim is, therefore, to bring the point of the needle in close contact with a low-threshold unit which can be recorded without disturbance. The point of the needle should not lie outside the muscle, nor in areas which are silent owing to pathological changes.

An unsuitably placed needle electrode gives no more information than can be recorded with pad electrodes, as exemplified by Fig. 1. This record is taken from a severe case of progressive muscular dystrophy (Case 1) from the greatly atrophied first interosseus muscle. Contractile tissue could scarcely be palpated, and there were no visible movements of the fingers when an attempt was made to spread them out. The needle position was first adjusted so as to obtain isolation of the action potentials (record a), of which a detailed picture is presented in record d. The number of units was greatly reduced. Only two or three are repetitive, with a frequency of 30 per second and occasionally up to 50 during maximal contraction. The high frequency is a good check that the person examined is doing his best to contract the muscle.

If (record b) the position of the needle is gently shifted a few millimetres, the base line becomes disturbed. The fine, distinct action potentials which repeat with a fairly constant amplitude are to an increasing degree replaced, even in minimal contraction, by broad, irregular potentials. If the patient makes a maximal contraction, they may have a rather large amplitude (Fig. 1c). This interfering activity fails to give the information that the muscle examined has a greatly reduced number of active units (Fig. 1a), as well as rapidly passing spikes with a duration of about one millisecond (Fig. 1d), and is therefore valueless for the purpose of differential diagnosis. Unless this fallacy is recognized one is liable to draw erroneous conclusions, for if the needle is not properly placed this same type of interfering activity may be seen also in the normal muscle and in cases of severe neurogenic lesions even on weak contraction.

Progressive Muscular Dystrophy.—Commencing in the most advanced stages of progressive muscular dystrophy a wasted muscle may appear to be electrically silent. If it is systematically searched, however, islands with greatly reduced activity are usually found, a few action potentials being brought into operation on maximal contraction (Fig. 1a). The spikes then have a very short duration, about 1 millisecond (Fig. 1d), that is, they are nearly as rapid as a motor nerve fibre spike potential. A few broader spikes may, however, remain. The occurrence of a relatively large number of very rapid action potentials is the most characteristic and constant change in the dystrophic muscle.

If the pathological process is somewhat less severe, several active units will be left which are sufficiently numerous to disturb the whole base line, although the largest spikes can still be followed separately in maximal contractions (Figs. 2 and 3).

Fig. 2 from the biceps muscle (Case 5) shows a voluntary contraction gradually increasing in strength. The activity starts with a small spike having an amplitude of 50 microvolts and a frequency of 14 per second (record a). The following three or four units (Fig. 2b) have an amplitude that must be regarded as pathologically small, that is 50 to 100 microvolts. In a normal biceps the units recruited as Nos. 2 to 4 would have had an amplitude of at least 100 to 500 microvolts. These small spikes all have a duration of about 1 millisecond. They are evidently identical with the action potentials which are indistinguishable from fibrillary spikes as reported in Bowden and Gutmann's case. The next unit recruited (record b) has an amplitude of 400 microvolts and a duration of 1 millisecond (record d). It can be followed on maximal contraction (record c), in spite of the interfering activity on the base line. The maximum frequency attained is 60 per second. The biceps muscle examined was greatly atrophied, about 1 cm. in diameter, and markedly paretic, though the degree of paresis could not be exactly determined, as the brachialis anticus was relatively intact.

The activity recorded in Case 4 (Fig. 3) shows the same general features. There are no abnormally small spikes, but all have a duration of 1 to 2 milliseconds (record c). On maximal contraction (record b) the action potentials only just take up the whole base line; six or seven of them are recruited at the maximum frequency of 45 per second. This record is from the right quadriceps muscle. The patient, when sitting on a chair with the legs straight, could not lift the heel from the floor. A normal quadriceps would have exerted considerably greater force in a case where the whole

base line on the electromyogram had been taken up by action potentials, which indicates that the individual " units " represented by the spikes had been reduced in strength.

When a muscle is strong enough to perform a movement at the joint against weak resistance, the number of recorded units on maximal contraction generally appears to be normal (Fig. 4), so that with moderate contraction they cover the whole base line (record c). Thus, the number of spikes in the electromyogram is not a sensitive index of changes in the muscle due to dystrophy. The majority of the spikes, however, still have a duration of 1 to 2 milliseconds (records d and e). These rapid spikes are often numerous in muscles showing only a slight paresis and atrophy : thus, in a record from a biceps muscle (Fig. 5, Case 3) they numbered about 40 or 50 per cent. of all the spikes registered. This, however, is not a constant finding.

It is often difficult to see any pathological features in the electromyogram from a slightly paretic muscle in cases of muscular dystrophy. Moreover, as shown by Snodgrass and Sperry (1941), in the extensor digitorium communis there are action potentials in the normal muscle of very short duration. The occurrence of spike potentials with a duration of 1 to 2 milliseconds is thus not always a pathological feature. Normally however, they occur sparsely, except in the facial muscles, where they are relatively common. In normal muscle they have to be searched for among the majority of spikes which have a duration of 4 to 10 milliseconds.

In three cases out of six in this group there was such a marked reduction in the number of active " units " that " single discharges " were obtained on maximal voluntary contraction.

Still more often one can find " single discharges " in the relatively benign forms of muscle dystrophy where the pathological process is confined to a few muscle groups. In such cases the changes develop during a much longer period than in the malignant generalized forms of dystrophy. This is seen in three examples of the facio-scapulo-humeral type of Landouzy and Dejerine (1884) (Cases 7–9), and in one case of the scapulo-humeral form of Landouzy and Dejerine (1886) (Case 10), where the disease had been confined for fifteen years or more to the shoulder-girdle, the thigh, and the anterior tibial muscle groups.

In the anterior tibial muscles of these cases only a few action potentials were recruited on maximal contraction. In this respect the picture was of the type which hitherto has been considered characteristic of neurogenic lesions. The spikes however were only of about 1 millisecond's duration.

Late Distal Hereditary Myopathy.—This applies also to the following group which deserves a more detailed description. Cases 11 to 25 are examples of a late distal hereditary myopathy, a type briefly described by Welander (1946), whose cases I have had the opportunity of examining. A complete description of this disease is in the course of publication by Welander. The disease closely resembles peroneal muscular atrophy. It is characterized by a late onset. The muscles earliest and most severely involved are the intrinsic muscles of the hand ; next in order follow the extensors on the forearm, the short extensors of the toes, and the tibial and peroneal groups, the peroneal being usually less affected than the tibial. Mild subjective sensory disturbances occurring distally in the extremities were observed in one out of the fifteen cases examined. The progress of the disease is very slow. The late onset, at an age between 35 and 60 years, beginning in the upper extremities, as well as the absence of cramp, fascicular twitching, and more pronounced sensory disturbance, make it possible to differentiate the disease, with tolerable certainty, from the Charcot-Marie-Tooth type of muscular atrophy.

Distal myopathies of a somewhat different type have also been described by Milhorat and Wolff (1943).

In some of these cases the insertion of the needle was followed by a series of action potentials of the fibrillary type, which died away in a few seconds, and indicated an increased mechanical irritability, When voluntary activity was already lost in the muscle to be tested, " insertion activity " could not be obtained, this being, in contrast to the findings in neurogenic paralysis, where spontaneous and mechanical irritability may remain for many years after denervation of the muscle. It seems that in myopathies the mechanical responses disappear simultaneously with voluntary activity.

" Single discharges " were found in seven or eight of the fifteen cases examined (Figs. 6 and 7). In Fig. 6, from the anterior tibial muscle (Case 12), only two different spikes were recruited on maximal contraction. The larger one had a frequency of 30 to 50 per second and an amplitude of 700 microvolts (record a), and its duration was 1 millisecond (record b). The smaller unit could be detected only if the amplification was increased (record c). Its amplitude was pathologically small, being merely 25 microvolts, and its duration 1 millisecond.

In Fig. 7 from the short extensor of the toes (Case 14) 3 or 4 different " units " were recruited. Records a and b show the instability of the spike amplitude, so characteristic of these rapid spikes.

On voluntary contraction, the amplitude of the largest spike diminished rapidly, but by degrees, from 1·5 millivolts to 500 microvolts. The reason was presumably that the point of the needle had shifted, but a blocking of some fibres in the " unit " would have produced the same result (Hoefer and Putnam, 1939 ; Buchthal and Clemmesen, 1941 a).

As shown in Fig. 8 (from the first interosseus muscle of Case 12), the number of units is larger in the less affected muscles. Records a, b, c show the recruitment of spikes with an increasing amplitude as the contraction is intensified. The contraction is introduced by a small spike of 50 microvolts, followed in turn by units of 100 and 200 microvolts (record a) ; next comes one of 250 microvolts (record b), and finally a spike of 800 microvolts (record c). Thereafter the recruiting cannot be followed any further. All the action potentials have a duration of 1 to 2·5 milliseconds (record e). Although a considerable number of units were mobilized on maximal voluntary contraction (record d), the patient could barely move the second finger. In this case, therefore, the individual action potentials represent very much less muscle strength than in normal muscle. The same condition is exemplified by Fig. 9 from the first interosseus muscle (Case 15). Records b and c show the activity on maximal contraction at two different positions of the needle while the strength developed by the muscle barely sufficed to move the forefinger.

For the purpose of comparison with neurogenic lesions, the amplitudes of the action potentials were measured in the order in which they were " recruited " (see Table) as the contraction was intensified. Six cases with severe changes were selected. In all 6, the number of " units " was greatly reduced, so that " single discharges " were obtained. In this respect the picture was thus identical with that seen in moderate or severe neurogenic paresis. By way of comparison, the Table also shows the average of double determinations of six normal cases recorded from the same muscle, that is, five from the first interosseus and one from the peroneal muscle.

TABLE

Case reference and muscle tested	Order of Recruitment				
	1	2	3	4	5
Case 11 inteross. muscle ..	50	100	100	450	300
Case 12 inteross. muscle ..	50	100	200	250	800
Case 15 inteross. muscle ..	25	50	100	200	300
Case 16 ant. tibial muscle ..	50	100	300	600	—
Case 17 inteross. muscle ..	100	1,500	1,000	200	—
Case 18 inteross. muscle ..	50	150	200	2,000	600
Mean value ..	54	408	316	600	500
Range ..	25–100	50–1,500	100–1,000	200–2,000	300–800
6 normal cases					
Mean value ..	220	480	360	490	510
Range ..	100–500	250–800	50–500	100–800	100–800

Amplitude of spikes in order of recruitment in cases of late distal dystrophy and in normal cases. Amplitude in microvolts.

Dystrophia Myotonica.—In dystrophia myotonica, Cases 26–29, the electromyographic picture is the same as in progressive muscular dystrophy, apart from the specific myotonic changes analyzed by Lindsley and Curnen (1936), Denny-Brown and Nevin (1941), and Buchtal and Clemmesen (1941 b) in man, and by Brown and Harvey (1939) in myotonic goats.

Myasthenia Gravis.—It is also interesting to note that in myasthenia gravis, Cases 30–32, the paretic muscle shows an electromyographic picture in certain respects identical with that seen in progressive dystrophy. When the paresis is very pronounced, as exemplified by Fig. 10 a and b from an almost paralytic biceps muscle (Case 30), the number of action potentials is only moderately reduced. The largest spike in the record can be followed on maximal voluntary contraction, against a background of smaller action potentials covering the base line (record b). As shown by Lindsley (1935), the amplitude of the spikes tends to diminish on continued contraction, as is also seen in record a and b. When the muscle is paralytic (record d from the masseter muscle of case 32), only a few active units, with a small amplitude, are left. Prostigmin rapidly restores the electromyogram to a more normal picture. As in muscular dystrophy, the extremely rapid action potentials are observed when the paresis is pronounced (Fig. 10c).

LESIONS OF THE LOWER MOTOR NEURONE

Reinnervation.—The electromyogram in reinnervation is in certain respects very similar to that seen in myopathy. This is exemplified by Fig. 11 from a case (No. 33) of localized neuritis of the shoulder girdle of the type described for example by Spillane (1943). The record was taken six months after the onset of the disease which clinically paralysed left deltoid muscle. There was no spontaneous fibrillation, but the insertion of the needle evoked a vigorous outburst of fibrillary action potentials, which died away after about ten seconds. Parts of the muscle were electrically silent on voluntary contraction. In other places small action potentials (Fig. 11a) were elicited, with a duration of 1 to 2 milliseconds. When the position of the needle was moved, action potentials of larger amplitude (record c), though with the same duration (record d), could be observed. Moreover, there were numerous polycyclic action potentials (records b and e). These findings are in complete accord with those of Weddell and others (1944). Although numerous action potentials were brought into operation, the muscle was clinically paralysed. Thus, as in cases of dystrophy, we find for the most part rapid action potentials, representing less muscular power than the spikes in normal muscle. On the other hand numerous polycyclic action potentials and evidence of increased mechanical irritability do not appear in cases of muscular dystrophy.

From the clinical point of view, the somewhat similar pictures seen in muscular dystrophy and in reinnervation is of relatively little importance as the differential diagnosis generally follows from the case history.

Acute Peripheral Nerve Lesions.—The same remark applies to acute peripheral nerve lesions. In such cases the development of fibrillation, Denny-Brown and Pennybacker, 1938, ten to eighteen days after denervation but not seen in reversible ischemic block, Weddell and others, 1944, is an extremely valuable sign. The voluntary action potentials are reduced in number, according to the degree of paresis. The duration and amplitude of the spikes usually lie within normal limits, as exemplified by Fig. 12 which was recorded from a clinically almost paralysed deltoid muscle (Case 34), examined 10 days after the onset of paresis. The duration of the single spike (record c) was 4 to 5 milliseconds, which is considerably greater than that observed in dystrophies. There was no fibrillation. Clinically, there was some suspicion of " psychogenic paresis." The frequency of discharge on maximal contraction, however, was 50 per second (records a and b), which shows that the patient, despite the great weakness of the muscle, had made a great effort to contract it.

Lesions of the Anterior Horn Cells.—In lesions of the anterior horn cells (amyotrophic lateral sclerosis, poliomyelitis, syringomyelia, compression of the spinal cord, etc.), and in certain cases of polyneuritis, peroneal muscular atrophy, inveterate peripheral nerve lesions with incomplete reinnervation, and herniated nucleus pulposus, there is another type of electromyogram, of considerable importance in differential diagnosis.

Spontaneous fibrillation, according to my experience, may often be absent in this group. When paresis is slight no decrease in the number of action potentials on maximal voluntary contraction can be detected. They take up the whole base line and interfere with one another. However, the spike amplitude is often unduly large, at any rate as regards the third and the following action potentials. This valuable sign can be seen even in muscles which, on clinical examination, appear normal. A detailed study of the spike amplitude will be published later and a typical example may be sufficient here.

Even when the paresis is only moderate, the number of spikes is distinctly reduced and they barely take up the base line. Reduction to this extent thus occurs earlier than in muscular dystrophies with a similar degree of paresis. This is exemplified by Case 35 (Fig. 13), where the patient was suffering from peroneal muscular atrophy.

Record 13a (calibration 500 microvolts) from the moderately paretic muscle of the right calf shows that the number of action potentials is so reduced that they do not cover the base line on maximal contraction. The amplitude of the spike with which the voluntary contraction starts is 500 microvolts; the next 5 millivolts; the third 3 millivolts; the fourth and last 12 millivolts. If we compare these amplitudes with the normal values in the Table, it will be found that they are much larger.

One should guard against mistaking action potentials evoked by the mechanical irritation of the needle for voluntary spikes. The mechanical irritability in denervated muscles is usually very marked, and a minor movement of the point of the needle owing to muscular contraction often suffices to elicit fibrillary action potentials or spikes with a greater amplitude and duration. Sometimes the slight movement in the point of the needle that occurs when an adjacent unit contracts may suffice to evoke them. The repetitive action potentials of the fibrillary type (record 13d) or the larger ones (record c) following the voluntary action potentials

with a " latency time " of 20 to 100 milliseconds are most easily explained in this way. Repetition in the same unit as is innervated or in adjacent units, evoked by excitation of the action potential, is less probable. At any rate they should not be viewed as voluntary spikes. In that case they might easily be interpreted as spikes of the dystrophy type, seeing that their duration is usually shorter than normal.

Discussion

The most important new fact which has emerged from this electromyographic study is the early change in cases of primary myopathy consisting of the occurrence of an abnormally large number of very rapid action potentials with a duration of about 1 millisecond. These seem to be produced by the gradual shortening of the duration of the normal action potentials and presumably represent the final stage in this process.

The other changes in the electromyogram are an inconstant diminution in the amplitude of the spikes and a reduction in their number, which is clearly noticeable only when there is marked paresis of the muscle tested. As shown by Figs. 8 and 9, the number of action potentials remaining may be considerable, even in muscles which appear to be almost paralysed.

In such cases they represent much less muscular power than the average action potentials in normal muscle.

All these changes in the electromyogram are most easily explained on the assumption that the number of muscle fibres belonging to the " units " are gradually diminished by the pathological process. The " units " eventually are completely destroyed, but not all of them at the same time, and some are more resistant than others. Whether the process is connected mainly with the small spikes which start the voluntary contraction (Smith, 1934), and which were thought by Denny-Brown and Pennybacker (1938) to represent small units controlling a few muscle fibres, and have been shown by Kugelberg and Skoglund (1946) to be innervated by low-threshold nerve fibres, or whether the process is connected with the larger high-threshold spikes, could not be determined. The degenerative process, however, seems to be rather diffuse. When the number of spikes in the myogram is distinctly reduced, the remaining action potentials as a rule are also profoundly changed in that the duration is shortened both of the spikes activated at an early stage in contraction, and of those activated only after intense contraction.

The electromyographical picture of dystrophies seems to correspond with the histological changes described, for example, by Pappenheimer (1908), Slauck (1921, 1932), and Bowden and Gutmann (1946).

It is not surprising that the electromyogram in muscular dystrophies should show changes very similar to those in cases of myasthenia gravis. As shown by Lindsley (1935), Harvey and Masland (1941), Harvey and others (1941), Harvey and Lilienthal (1941), the paresis is caused by a neuromuscular block. One muscle fibre after the other is blocked in the unit ; and, though this process is functional and reversible, its result will be essentially the same as if an increasing number of muscle fibres were put out of action in the unit by other more profound changes, as in muscular dystrophy.

It is, moreover, evident that the electromyographical picture in reinnervation must in some respects be identical with that in myopathies. All the muscle fibres in a " unit " cannot, of course, be reinnervated at the same time. The unit must, therefore, to begin with, consist of an abnormally small number of muscle fibres. Just as has been found to be the case in myopathies, the power of the muscle on maximal voluntary contraction will be poor despite the fact that many units are brought into operation. The individual action potentials tend to become more rapid and of lower voltage than the normal ones.

Myopathies affect individual muscle fibres, whereas lesions of the lower motor neurone affect whole " units." The destroyed unit belonging to one nerve fibre is put out of action at once and not gradually. If we have, say, 100 nerve fibres innervating 100 units, each composed of 100 muscle fibres, and destroy 90 per cent. of the nerve fibres, the number of units and the muscular power will be reduced to one tenth of the original. In myopathy, if 90 per cent. of the muscle cells had been uniformly destroyed in all units, the muscular power would likewise have been reduced to one-tenth, but the number of functioning units would have remained unchanged.

A decrease in the number of spikes relative to the loss of muscular power occurs, therefore, much earlier in neurogenic than in myogenic lesions. However, as shown above, units are not always destroyed uniformly in cases of myopathy, though eventually there is a considerable reduction in their number, so that " single discharges " are obtained on maximal voluntary contraction. This occurs most often in localized forms of myopathy, which, clinically, may show great similarity to certain neurogenic diseases. In such cases the number of spikes in the electromyogram relatively to the degree of paresis cannot serve as a basis for the differential diagnosis. Moreover, fibrillary twitchings

are often absent in chronic neurogenic complaints such as those of the Charcot-Marie-Tooth type. For the differential diagnosis in such cases, we are thrown back upon the characteristic changes undergone by the action potentials with respect to duration and amplitude. This applies also to the recognition of the early stages of the motor neurone disease, when the paresis is so slight that the reduction in the number of action potentials is not yet observable. In this way a clear-cut differential diagnosis between myogenic and neurogenic lesions can be made.

Summary

The typical electromyographical sign of myopathies is the occurrence of spike potentials with an abnormally short duration. "Single discharge" waves also occur: these cannot, therefore, be regarded as pathognomonic for neurogenic lesions. In myopathies the spikes in "single discharges," however, have an approximate duration of 1 millisecond, as against a duration of 5 to 10 milliseconds in neurogenic lesions (except in reinnervation).

1. In muscular dystrophy (6 cases of the proximal type, 4 of the Landouzy and Dejerine form, and 15 of a distal type with late onset), the earliest observable change, visible even in mild or moderately severe paresis, consists of a large number of spikes with a duration of about 1 millisecond. Intensification of the paresis is manifested by an increase in the relative number of rapid spikes, which at the final stage comprise all or most of the remaining action potentials. They represent a degree of strength which is much less than that of the average action potential in the normal muscle. The amplitude of the spikes may show an irregular reduction relative to normal.

A reduction in the number of action potentials on voluntary contraction is clearly noticeable only when the paresis is marked. When the muscle is scarcely able to perform a movement in the joint, the spikes can be followed separately on maximal contraction. They then barely take up the whole base line on the electromyogram. When the paresis is still more pronounced, only a few action potentials remain, or the muscle may even be electrically silent.

The changes in the electrical activity are explained by the pathological process which throws one muscle fibre after another out of action. This proceeds fairly uniformly in the different muscle "units," though some of them are somewhat more resistant than others.

2. In dystrophia myotonica (4 cases) the voluntary action potentials in the atrophied muscle undergo essentially the same changes as in muscular dystrophy. The same remark applies to myasthenia gravis (3 cases), where the muscle fibres are put out of action in the "units" by a functional and reversible process.

3. With special regard to differential diagnosis, certain characteristic changes in the electromyogram in lesions of the lower motor neurone are discussed, and contrasted with the electrical changes in myopathy.

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For illustrations to this article see pages 129-133

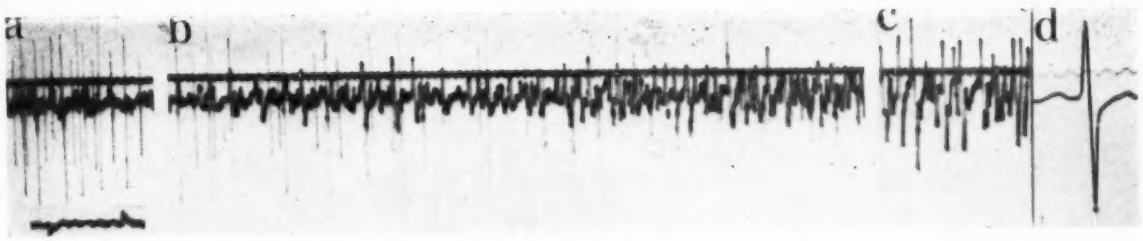

FIG 1.—Muscular dystrophy (Case 1). Records from the first interosseus muscle. *a.*—Maximal voluntary contraction with properly placed needle electrode, showing perfect isolation of the action potentials which are reduced in number. *b and c.*—Needle is gently shifted a few mm. as contraction is going on. The distinct spikes are replaced by interfering activity of no diagnostic value. *d.*—Detail picture of a typical dystrophy spike with a duration of about 1 millisecond.

In this and the following figures : calibration 100 microvolt (except Fig. 15a). Time 1/100 sec. In detail pictures of single spikes, time 1/1,000 sec.

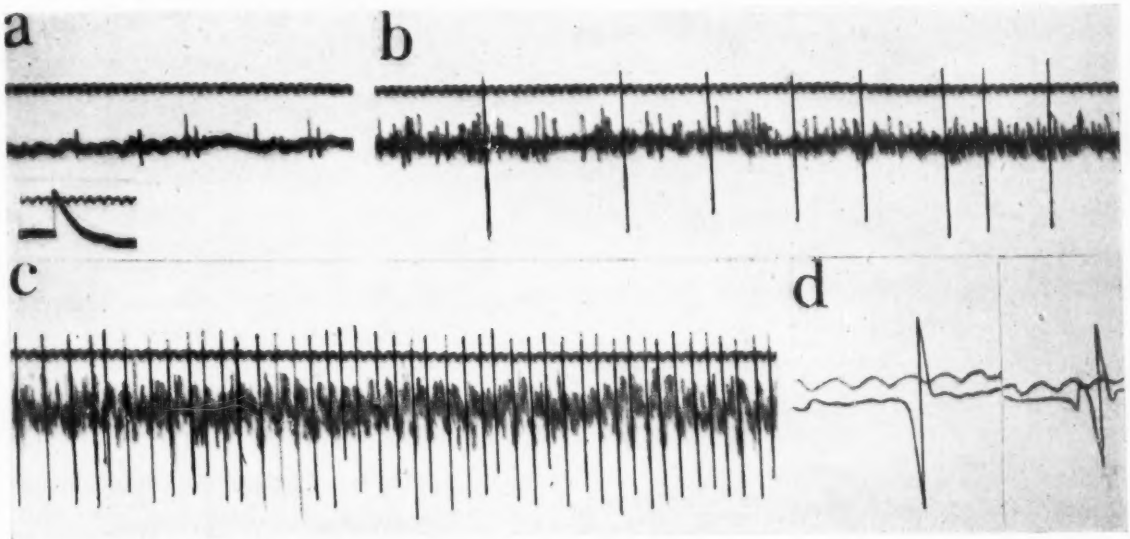

FIG. 2.—Muscular dystrophy proximal form (Case 5). Records from the greatly atrophied biceps muscle. *a, b,* and *c.*—Showing the activity of a voluntary contraction gradually increasing in strength. In *d* a detail picture of the largest action potential seen in *b* and *c.*

FIG. 3.—Muscular dystrophy (Case 4). Records from the highly paretic quadriceps muscle.

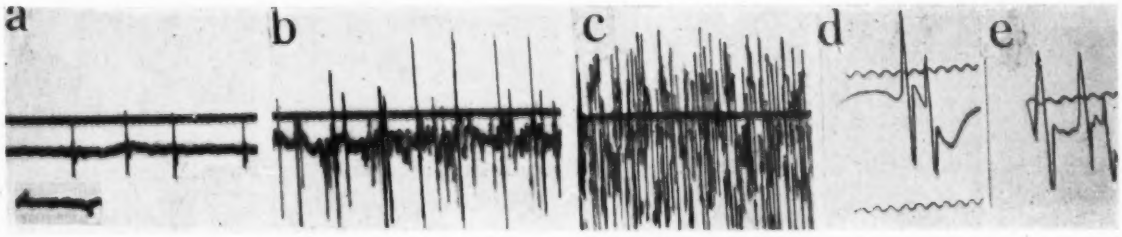

FIG. 4.—Muscular dystrophy (Case 2). Records from the moderately paretic quadriceps muscle.

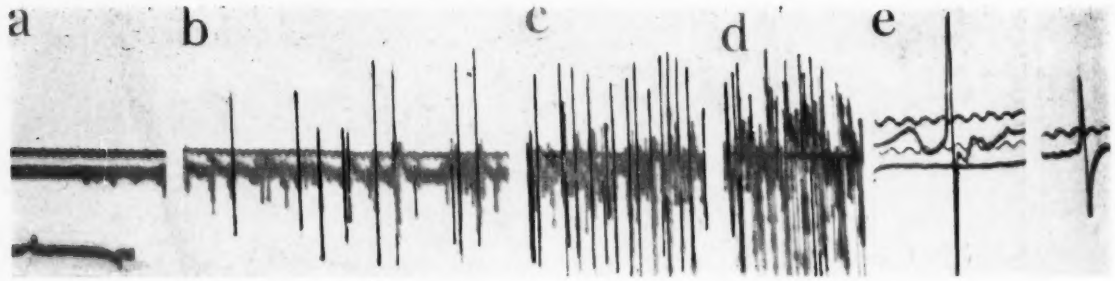

FIG. 5.—Muscular dystrophy (Case 3). Records from the slightly paretic biceps muscle.

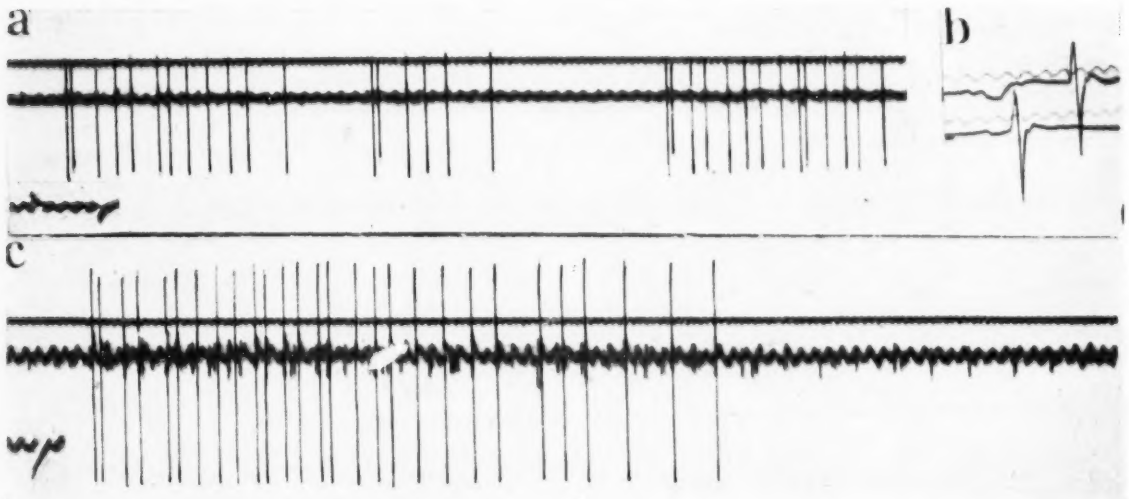

FIG. 6.—Late distal type of myopathy (Case 12). Records from the clinically paralytic anterior tibial muscle.

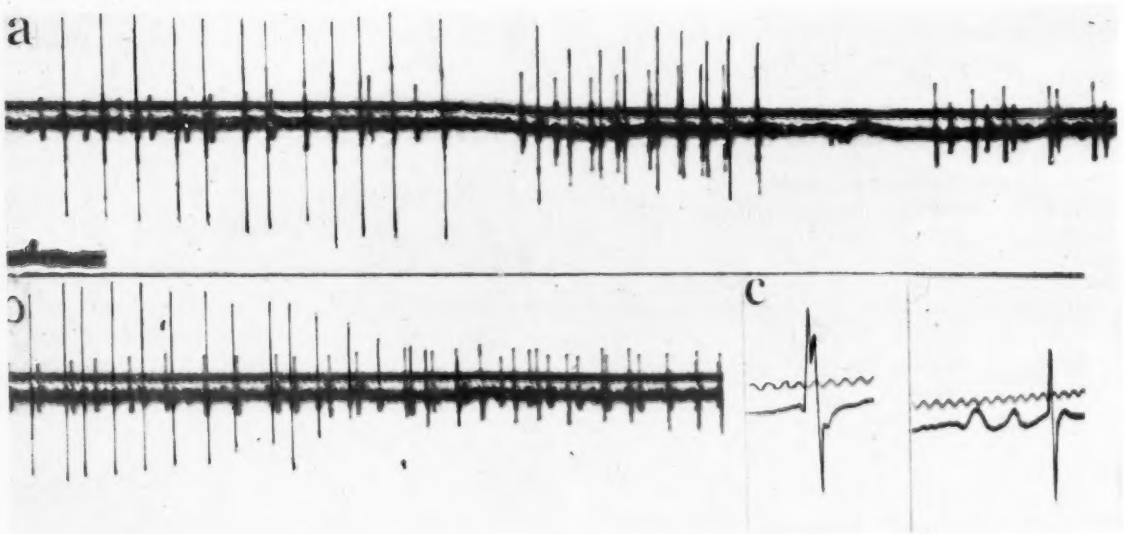

FIG. 7.—Late distal type of myopathy (Case 14). Records from the short extensor muscle of the toes.

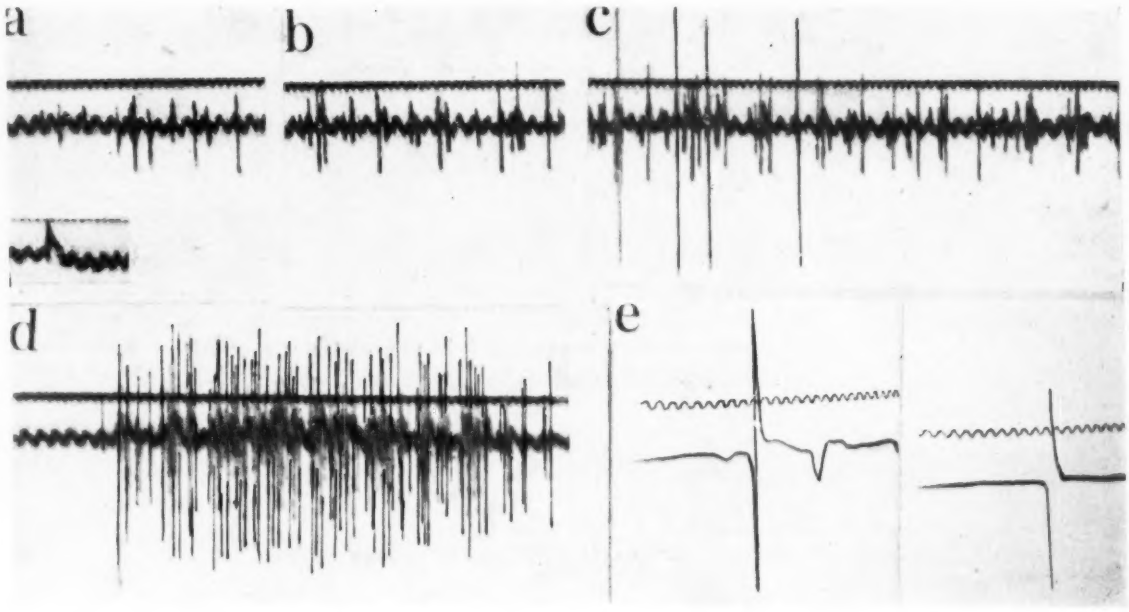

FIG. 8.—Late distal type of myopathy Case 12). Records from the first interosseus muscle which could barely move the second finger.

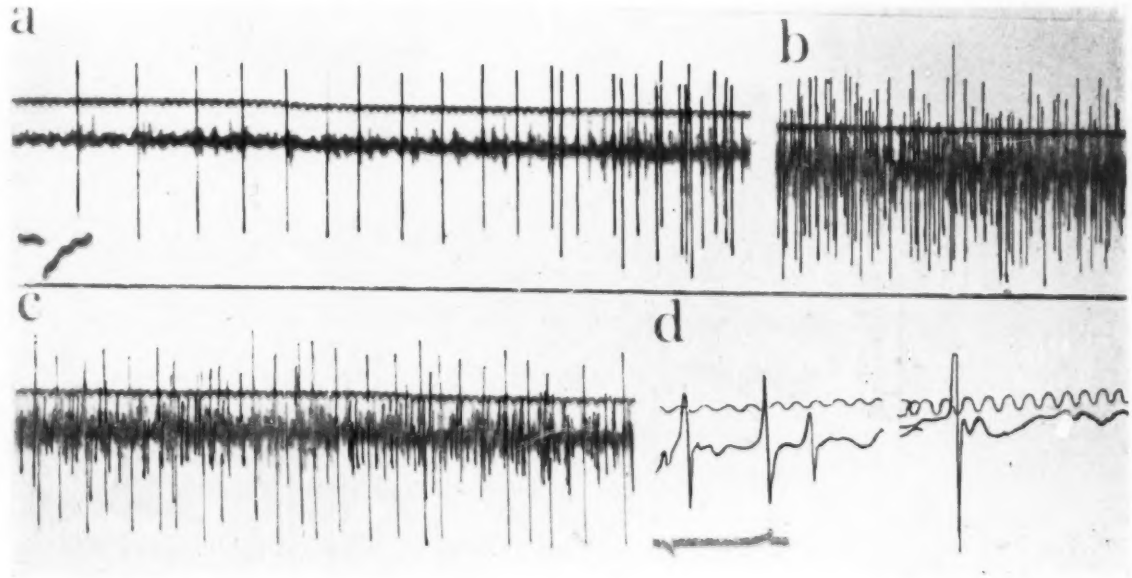

FIG. 9.—Late distal type of myopathy (Case 15). Records from the highly paretic first interosseus muscle.

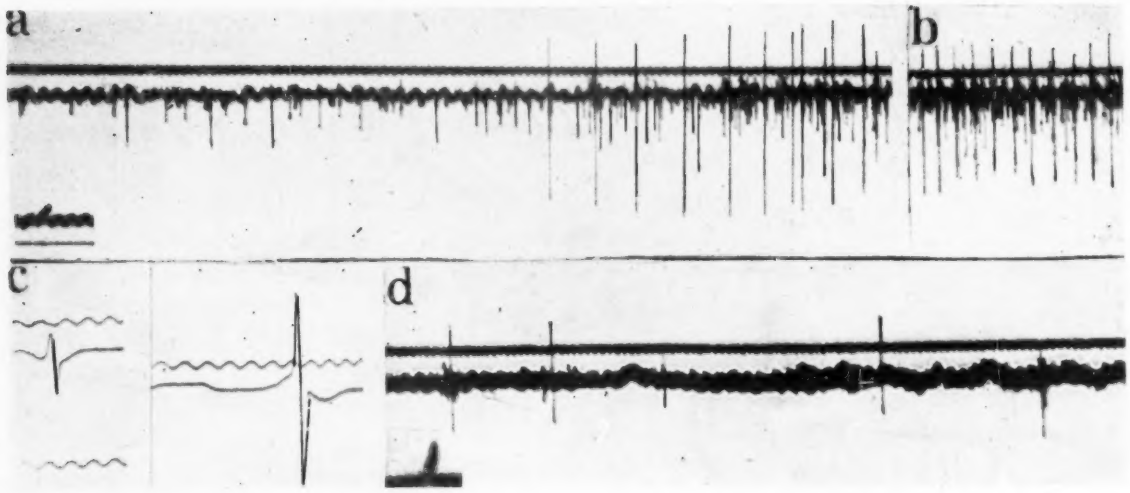

FIG. 10.—Myasthenia gravis. Records *a*, *b*, and *c* from an almost paralytic biceps (Case 30). Record *d* shows the activity from a paralysed masseter muscle on maximal voluntary contraction (Case 32).

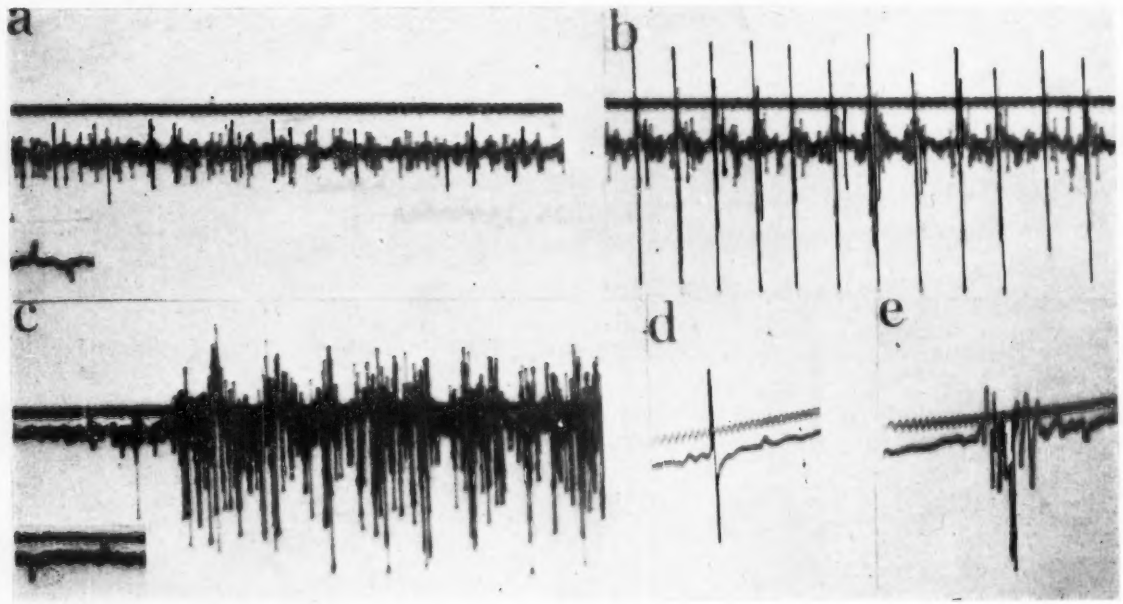

FIG. 11.—Localized neuritis of the shoulder girdle (Case 33). Records from the deltoid muscle showing reinnervation activity.

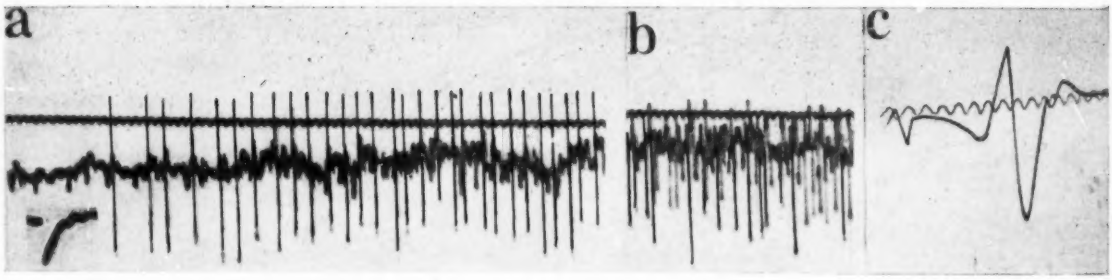

FIG. 12.—Acute peripheral nerve lesion (Case 34). Records from the clinically almost completely paralysed deltoid muscle.

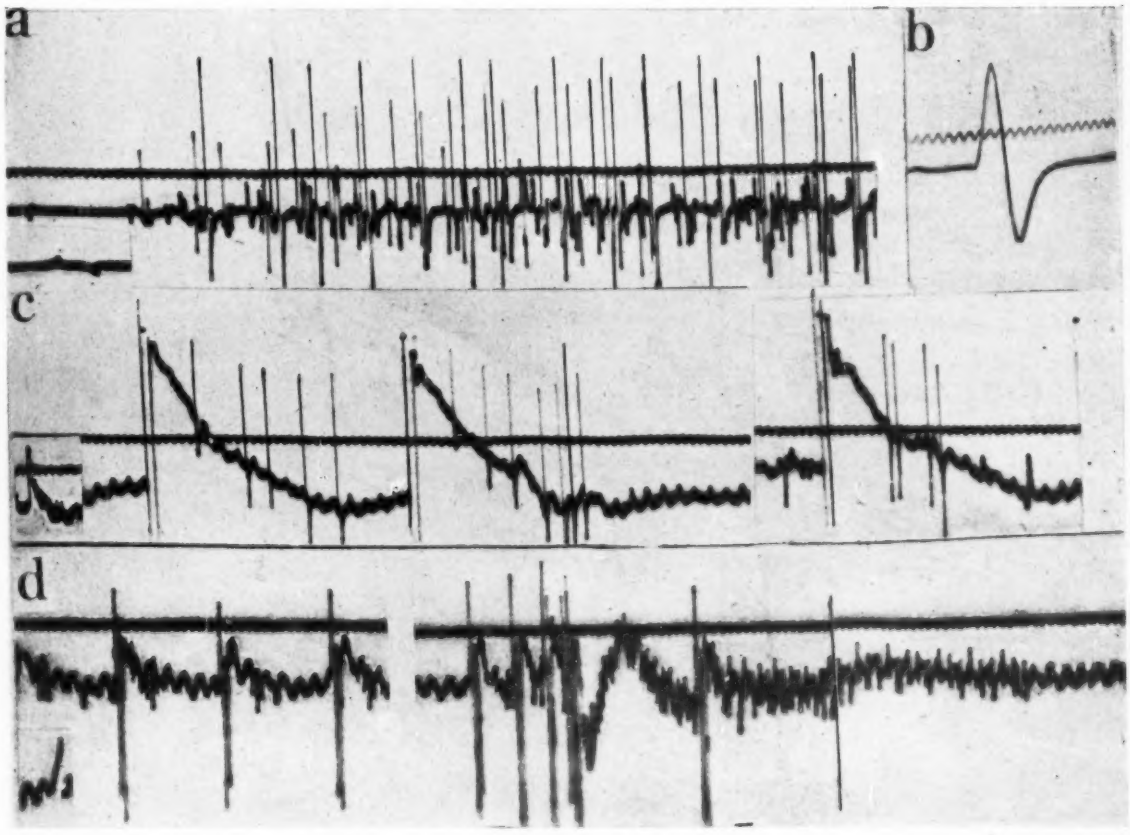

FIG. 13.—Peroneal muscular atrophy (Cases 35 and 36). Records from the moderately paretic calf muscle. *a*.—Calibration 500 microvolts. Shows a voluntary contraction increasing to maximal strength. The action potentials are reduced in number and of pathological large amplitude. *b*.—Detail picture of one action potential. *c*.—Larger amplification (calibration 100 microvolts). The voluntary spikes which are too large to be registered correctly at this amplification are followed by repetitive spikes of shorter duration and smaller amplitude. *d*. (Case 36).—The voluntary action potentials are followed by repetitive spikes of the fibrillary type. The base line is somewhat disturbed by 50 cycles per second alternating current.

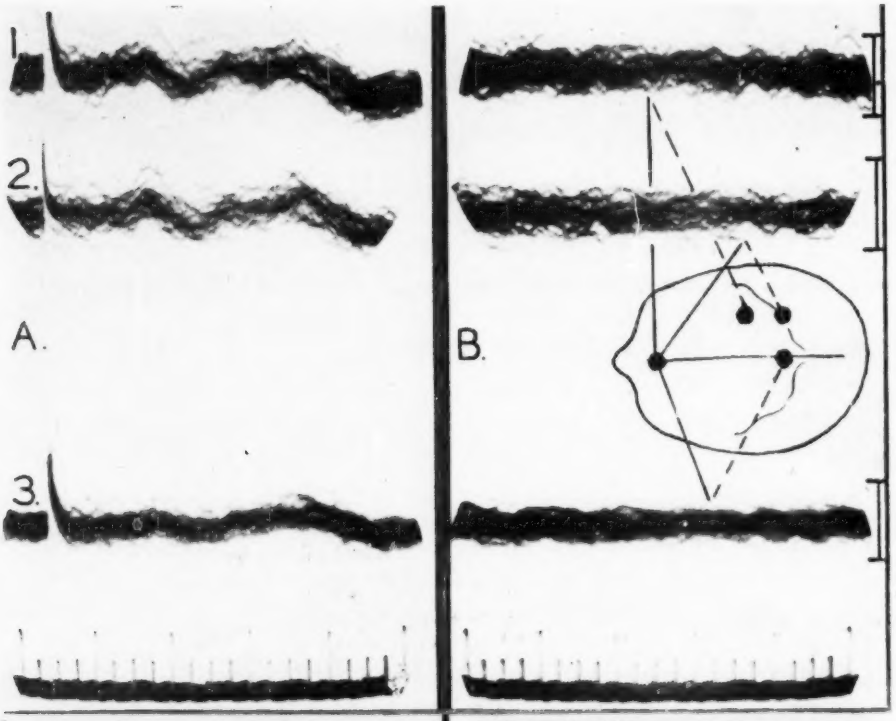

FIG. 1.—In (*a*) are shown, superimposed, fifty responses to stimulation of the left ulnar nerve at the wrist. The stimulus escape at the left-hand end of the record is followed by a train of waves each with a period of about 20 msecs. In (*b*) the potential differences between the same electrodes on the head have been recorded but no stimulus has been applied. No deflections comparable with those in (*a*) occur. The time scales show intervals of 5 and 20 msecs. Calibration marks at the right-hand end of (*b*) show the deflection produced in each channel by a potential difference of 20 μV.

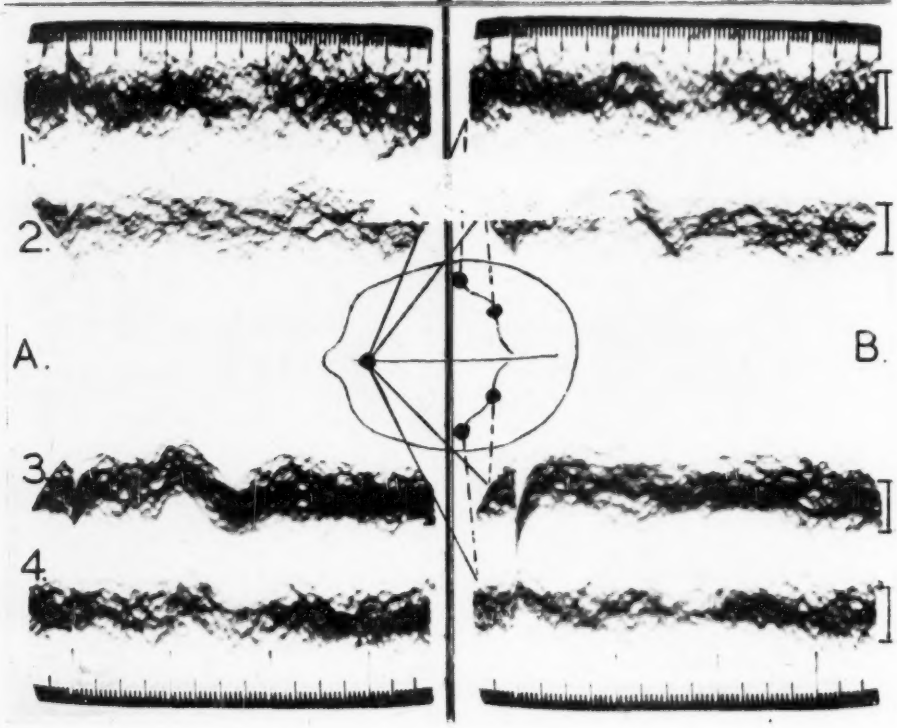

FIG. 3.—The records show the responses to stimulation of the ulnar nerves at the elbow. In (*a*) the stimulus is on the right side and the only visible responses appear in leads 3 and 4 from the left hemisphere. In (*b*) the stimulus is applied to the left side and the response is only apparent in leads 1 and 2 from the right side of the head. The posterior electrodes are 7 and 14 cm. from the midline and in each case the response is largest in the lead from the electrode 7 cm. from the midline. The calibration lines at the end of (*b*) represent 20 μV.

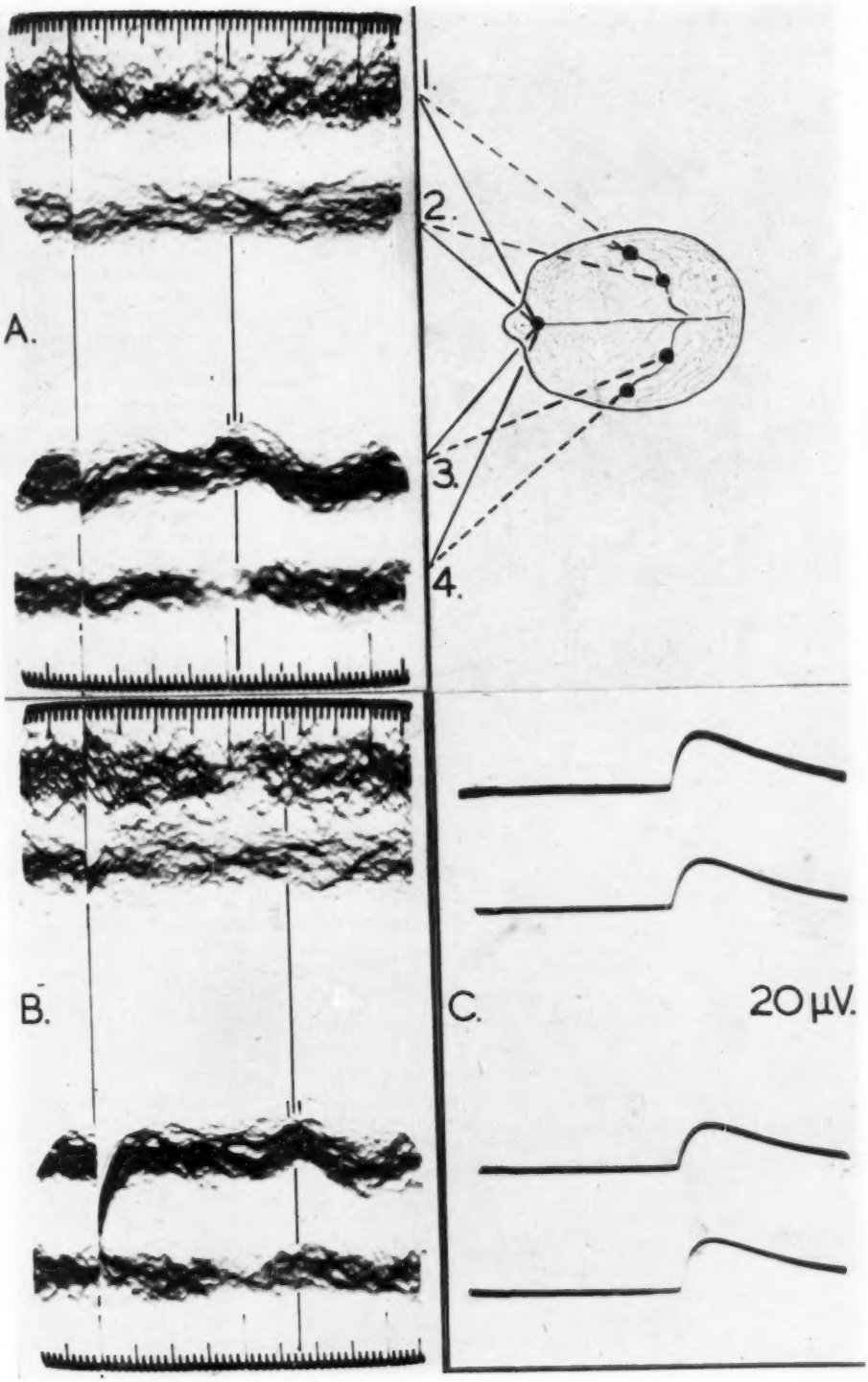

FIG. 2.—The records show the responses to stimulation of the right ulnar nerve. In (*a*) the stimulus has been applied at the elbow and the latency from the stimulus to the peak of the response is 22 ± 1 msecs. In (*b*) the stimulus has been applied at the wrist and the latency is 28 ± 1 msecs. (*c*) shows a record of fifty superimposed deflections due to a rectangular step input to the amplifiers of 20 μV. This record indicates the amplifier frequency response used in these experiments and the small contribution of the amplifier irregularity to the thickness of the baseline in the records shown in (*a*) and (*b*). The time scales in this and all following records show 1, 5, and 20 msec. intervals.

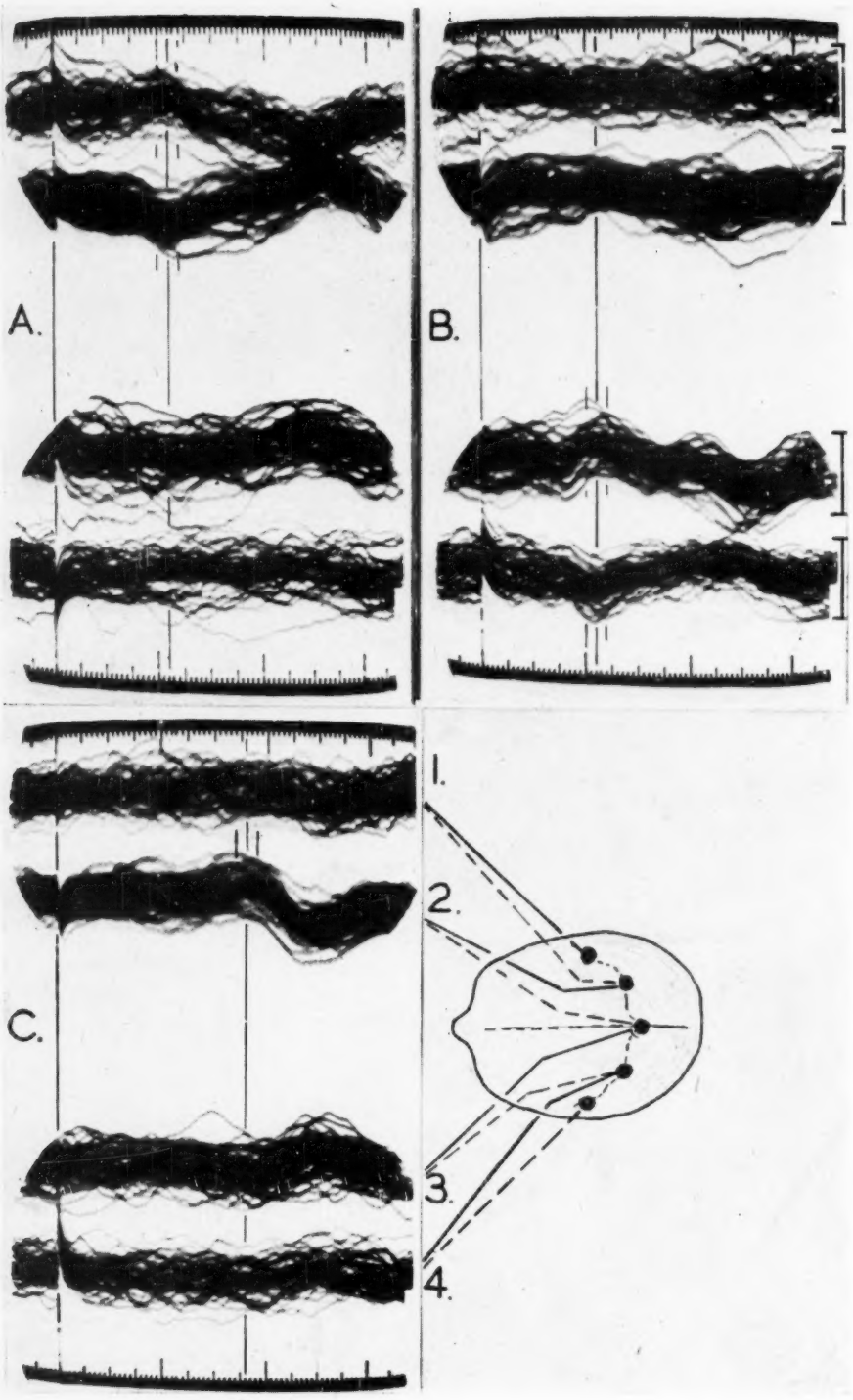

FIG. 4.—The records show the responses to stimulation of the left and right median nerves at the elbow and the left lateral popliteal nerve at the head of the fibula. The electrodes are applied over the surface markings of the sensory-motor areas in the midline and 6 and 12 cm. from it on each side. A stimulus to the left median nerve (*a*) produces a potential change maximum near to the electrode on the right side common to leads 1 and 2, 6 cm. from the midline. A stimulus to the right median nerve (*b*) produces a similar disturbance on the left side of the head. Stimulation of the left lateral popliteal nerve gives rise to a potential change occurring nearer to the midline electrode than to any of the others, but not symmetrically disposed with respect to it. The latency of the response to stimulation in the leg is 36 ± 2 msecs., about 14 msecs. longer than in (*a*) and (*b*). The calibration marks show a potential difference of 15 μV.

CEREBRAL RESPONSES TO ELECTRICAL STIMULATION OF PERIPHERAL NERVE IN MAN

BY

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(RECEIVED 30TH JULY, 1947)

Introduction

EXPERIMENTS to be described elsewhere have shown that in a patient suffering from myoclonic seizures electrical stimulation of peripheral nerve resulted in changes of electrical potential detectable on the scalp. These changes in potential difference were largest over the hemisphere on the side opposite to that stimulated. They were located near to the midline when the lateral popliteal nerve in the leg was stimulated and more laterally when the ulnar nerve was stimulated in the arm.

The experiments to be described in this paper have been made to find out if any action potentials may be detected in healthy subjects comparable with those found in the patient with myoclonus. Evidence will be presented to support the suggestion that potential changes of cerebral origin, which probably arise in the central or postcentral cortex, may be detected on the scalp in healthy subjects following electrical stimulation of peripheral nerves.

Methods

The stimulus used was an electric shock with a rapid rise and a decay of exponential form with a time constant of 50 microseconds. The cathode, a 1 cm. diameter pad soaked in salt solution and mounted on a chloride-coated silver rod, was applied to the ulnar nerve at the wrist or elbow, to the median nerve at the elbow, or to the lateral popliteal nerve at the head of the fibula. The anode was a saline-soaked pad large enough to cover the back of the hand and applied either there, to the forearm, or to the calf of the leg. Neither of the stimulating electrodes was earthed, and the stimulus was applied to them through a Muirhead wide-range transformer. An earth connexion was made the to subject, usually to the upper part of the chest or on the limb stimulated proximal to the stimulating electrodes. The stimulus was adjusted in size to be maximal or supramaximal for the motor fibres in the nerves stimulated. It was applied once a se ond by a trigger circuit locked to a fixed point on the sweep of a cathode ray oscillograph. Fifty or more successive sweeps were photographed superimposed in a single record. In such a record any waves which follow the stimulus by a regular interval will all occur at the same place on the trace ; they may thus be detected although they are no larger than the deflections produced by spontaneous activity of the brain and scalp muscle. As deflections due to these causes are not regularly related to the stimulus, they tend to occur at a different place on each successive sweep and therefore appear only as a thickening of the baseline. High contrast obtained in the photographic processing makes clearer the places where a number of sweeps have superimposed exactly. The time scales on the records show 5 and 20 millisecond intervals in Fig. 1 and in all other figures intervals of 1, 5, and 20 msecs. In the earlier experiments these time scales were derived from the 50 c/s. supply mains but in later experiments, for reasons connected with the exclusion of artefacts which will be discussed later, they were derived from a quartz crystal oscillator. The sizes of the calibration marks on the records are indicated below each figure. All records read from left to right.

At first the scalp potentials were picked up with saline-pad electrodes. For reasons of comfort in the later experiments, which tended to be longer, silver-cup electrodes were fixed on with collodion. The cups were 1 cm. in diameter, coated with silver chloride and filled with Cambridge electrode jelly. The electrode placements used are indicated in the figures. The amplifiers were connected in such a way that, if in any channel the electrode shown connected to the continuous line became negative with respect to that shown connected to the broken line in the head diagrams, an upward deflection would result in the record from that channel. The potential differences were amplified with conventional resistance-capacity coupled amplifiers and recorded photographically from Cossor double-beam cathode-ray oscillographs. The frequency response of the amplifiers was restricted so that they attenuated, with respect to the level at 35 c/s., by 50 per cent. at 180 c/s. and by 20 per cent. at 10 c/s. This restriction of the frequency response must have affected the form of some of the waves recorded. Therefore little importance has been attached to waveform in these studies, though experiments with less restricted frequency responses suggest that the distortion is not gross. No resonant circuits have been used to restrict the frequency response, and therefore any periodic waves in the records are not due to the excitation of such circuits by spread from the stimulus or any other regularly occurring disturbance.

The subjects were examined in the supine position

with the head supported in such a way as to relax the neck muscles. During the periods of stimulation the eyes were kept open or closed, whichever reduced to the greatest extent the combination of spontaneous brain activity, scalp muscle activity, and blinking, all of which thicken the baseline.

Material

Fourteen subjects have been examined. All were healthy males between the ages of 26 and 50 years. No drugs were given and no abnormal conditions were present at the time of the examinations.

Results

In twelve of the fourteen subjects examined it has been possible to detect a change of potential over the surface marking of the contralateral sensory area following stimulation of peripheral nerves.

Fig. 1A (p. 134) is a photograph of the superimposed responses to fifty successive stimulations, at one second intervals, of the left ulnar nerve at the wrist. The record shows a series of small but definite waves following the initial rapid deflection due to spread from the stimulus. The first clearly discernible wave begins 22 to 23 msecs. after the stimulus and the first peak occurs 25 to 27 msecs. after the stimulation. The sense of the deflection of the first phase of the waves indicates that the more posterior electrodes became positive with respect to the common electrode at the nasion. The deflections are greatest in leads 1 and 2, from the electrodes lateral to the midline, and least in lead 3, from the electrode on the midline. This difference in the deflections in the different leads suggests that the disturbance did not occur under the frontal electrode common to all three channels. Fig. 1B shows fifty successive sweeps recorded under the same conditions as in Fig. 1A but without any stimulus applied to the nerve. No comparable deflections occur, and it may therefore be suggested that the waves following the stimulus in Fig. 1A were provoked by that stimulus and were not spontaneous. Before it can be decided that such waves are of cortical origin several sources of artefact must be excluded.

The period of the waves in Fig. 1A is near to 1/50th of a second, and it is therefore necessary to show that they are not due to any form of pickup from the 50 c/s. supply mains. In Fig. 1B, where no stimulus was applied, there is some evidence towards the end of the trace of a small oscillation with a frequency of 100 c/s., which may well have had such an origin. The time scale in these first records was derived from the 50 c/s. supply mains, and to obtain superimposition of the time marks in the successive sweeps the recurrence rate of the sweep had necessarily to be an exact sub-multiple of the mains frequency. Therefore waves related integrally to the supply frequency superimposed accurately. To avoid this difficulty due to interference from the mains the sweep was in all later experiments locked to a sub-multiple of 50.00 c/s. derived from a quartz crystal oscillator which also provided the time scale. It is usually possible to record at a time when the frequency of the mains is not exactly 50 c/s. At such a time no two waves due to potentials derived from the mains will superimpose exactly, except at long intervals, and consequently they will appear as a thickening of the baseline and not as a regular wave. Thus any waves which superimpose accurately in successive sweeps cannot be derived from the mains if these have a frequency of other than 50 c/s. at the time the record is made. Using this method it is possible to say that the waves following the stimulations in the later records were not due to any form of interference from the supply mains.

The next source of artefact that must be excluded is spread of the stimulating current. The potential difference between the stimulating electrodes in these experiments was between 50 and 80 volts ; and it is not always possible to avoid all spread of current to the recording electrodes. That the train of waves following stimulation is not just a residual oscillation due to spread of the stimulus is suggested by the records shown in Figs. 2 and 4 (pp. 135, 136). The records in Fig. 2 were made from four electrodes, two over each sensory-motor region, and a fifth one common to all four channels at the nasion. Stimulation of the right ulnar nerve at the elbow, Fig. 2A, produced a response visible in lead 3, from the more medial of the two electrodes on the left side of the head. The interval between the stimulus and the peak of the first phase of the wave, indicated by the vertical lines through all four traces, is 22 ± 1 msecs. The short vertical lines over the peak of the wave indicate intervals of 1 msec. before and after the long line. In this and all later figures the stimulus was released at the time of the first 20 msec. marker in the time scale. Stimulation of the same nerve but at the wrist, Fig. 2B, produced a slightly smaller response in the same lead ; and the interval between the stimulus and the first peak of the wave is now 28 ± 1 msecs. This increase in the latency of the response by 6 ± 2 msecs. suggests that the response picked up on the scalp was more probably a correlate of a disturbance propagated in the nerve than of any purely electrical aftermath of the stimulus. The same is suggested by the records in Fig. 4A and C. In Fig. 4A a stimulus applied to the left median nerve at the elbow caused a response to appear in leads 1 and 2, from the right parietal region. The interval between the stimulus and the first positive peak of the wave is 22 ± 2 msecs. A stimulus to the lateral popliteal nerve

at the head of the fibula, Fig. 4C, was followed by a response appearing nearer to the midline, chiefly in lead 2 and to a less extent in lead 3. The interval between the stimulus and the first positive peak of the wave is 36 ± 2 msecs., an increase of the latency by 14 ± 4 msecs. over that of the response to stimulation of the median nerve at the elbow.

Another source of artefact, a reflex twitch of scalp muscle, cannot be excluded directly, but the locations of the responses to be described make it seem unlikely that this is their origin. For the location of cerebral action potentials through the intact skull the use of a single electrode common to all the amplifiers and as remote as possible from the active area, together with a number of electrodes near to the active area, is open to criticism. This method has, however, the advantage of picking up the largest possible potential differences and it has been used in the majority of these experiments. A more satisfactory method is that described by Adrian and Yamagiwa (1935), who plotted the potential gradients over the scalp. For this a number of electrodes in line are connected to the amplifiers in such a way that a disturbance under an electrode common to two channels produces a deflection in opposite sense in those two channels. Under these conditions, although the place at which the greatest potential change is occurring may be accurately located, the separation of the electrodes is smaller and the potential differences between them may be too small to be detected. Fig. 3 (p. 134) shows records made by the first method with the same electrode positions as those used in the records in Fig. 2. Stimulation of the right ulnar nerve at the elbow, Fig. 3A, produced a response that is largest in lead 3, from the more medial of the two electrodes on the left side of the head, 7 cm. from the midline. No response is evident in leads 1 and 2 from the head on the same side as the arm stimulated. Transferring the stimulus to the ulnar nerve of the left side, Fig. 3B, caused the response to appear largest in lead 2, from the more medial of the two electrodes on the right side of the head. No response was then evident in leads 3 and 4, from the left side of the head. It seems that in this experiment the response was largest about 7 cm. from the midline on the side of the head opposite to that of the arm stimulated. The second method of location was used in the experiment from which records are shown in Fig. 4. Here a line of electrodes was applied over the surface markings of the sensory-motor areas of the two sides. The lateral electrodes were 6 and 12 cm. from the midline. The record in Fig. 4A shows a deflection occurring in opposite sense in channels 1 and 2, from the right side of the head, when the left median nerve was stimulated at the elbow. This shows that the first phase of the response, with its peak 22 msecs. after the stimulus, was a disturbance that was greatest nearer to the electrode 6 cm. from the midline on the right side than to any of the other electrodes; also that in this phase of the response the active area became positive with respect to the parts of the scalp under the other electrodes. Stimulating the median nerve at the elbow on the right side, Fig. 4B produced a similar response but maximal about 6 cm. from the midline on the left side of the head. Fig. 4C shows records taken during stimulation of the lateral popliteal nerve at the head of the left fibula. Here the response is largest in lead 2 and of opposite sense, though much smaller in lead 3. This indicates that the disturbance occurred nearer to the midline electrode than to any of the others but was not symmetrically disposed with respect to this electrode.

In none of these healthy subjects who showed the response was it possible to pick up the potential changes more than two or three centimetres in front of or behind the surface markings of the central sulcus. The locations of the responses to stimulation of peripheral nerves, particularly that in which the response to stimulation of the popliteal nerve in the leg was located near the midline, where there is least scalp muscle, seem to indicate that the responses were probably not due to reflex twitches of scalp muscle.

Experiments on the subject with myoclonic seizures, to be described elsewhere, have shown that the response to a stimulus can be facilitated to the extent of 50 to 70 per cent. in size by the previous application of a conditioning shock 60 to 100 msecs. earlier. The period of facilitation is followed by a period in which the response to the test shock is depressed. Experiments were made with paired shocks in four of the healthy subjects in this series. So far no objective evidence of any facilitation of the response to the test shock has been found. However, each of the four subjects, although unaware of the results obtained with the others, or of the manner in which the interval between the stimuli was changed, described an alteration in the quality of the perceived sensation when the interval between the stimuli was between 70 and 100 msecs. The first subject stated that there was something wrong with the stimulator, since he was feeling four instead of two shocks, which he had reported at longer and shorter intervals. The other three subjects described the change in terms of a third weaker shock following the second of the pair. It seems, therefore, that the 60 to 100 msec. interval, in which facilitation of the response to a second stimulation occurs in the subject with myoclonus, may have some counterpart in normal cortical function, though no objective evidence of this has been found.

Discussion

It is suggested that the potential changes that have been picked up from the scalp following stimulation of peripheral nerves are in fact cerebral action potentials and that they arise in the central or post-central cerebral cortex. The short latency between the stimulus and the beginning of the response, of the order of 18 milliseconds following a stimulus at the elbow, suggests that the response indicates events occurring in the cortex at, or soon after, the time of arrival of the afferent volley at the cortex.

The failure to find a response to stimulation in two of the fourteen subjects examined was possibly due to the electrodes not being over the very limited area in which the response appears. That this was so is suggested by the fact that in one subject in whom no response was found in an earlier examination, a fuller investigation showed that a response could be detected. The same difficulty of locating the electrodes accurately over the centre of the disturbance may account for the difference in size of the deflections produced by the stimulation of the lateral popliteal nerve, Fig. 4C, and by stimulation of the median nerves, Fig. 4A and B. It might be expected that the response to the stimulation of the median nerves would be the larger of the two. Although the primary positive wave is less clear during stimulation of the lateral popliteal nerve than when stimulating the median nerve, the immediately succeeding negative change is considerably larger in the first instance. No significance may be attached to this difference since the electrode common to channels 1 and 2 on the right side, or to channels 3 and 4 on the left side, although well placed with respect to the active area in the coronal plane, may have been less favourably placed in the sagittal plane than was the midline electrode.

Comparison of the responses to stimulation of peripheral nerve described above with the potentials detected by Davis (1939) following auditory stimulation, and by Davis, Davis, Loomis, Harvey, and Hobart (1939) following electrical stimulation of a finger, is difficult on account of the differences in techniques used. The responses described by these authors had a latency of 30 to 40 msecs. and 40 to 100 msecs. respectively, and in both cases the duration of the response was described as of the order of 300 msecs. From these figures it seems unlikely that the mechanisms involved are closely related.

The relation of these responses to peripheral nerve stimulation, consisting of a group of two to four waves, each with a period of 15 to 20 msecs., and a peak amplitude on the scalp of 5 to 10 μV., to the potential changes that may be evoked from the cortex of animals by sensory stimulation is not clear on the evidence at present available. The polarity of the first phase of the wave in which the active area becomes positive with respect to other parts of the scalp, and its duration of 15 to 20 msecs., suggest that there may be some correspondence with the responses to electrical stimulation of a toe in the monkey after recovery from ether anæsthesia that have been described by Marshall, Woolsey, and Bard (1941). How the latencies of the responses correspond in the two cases may not be considered in the absence of more information about the lengths of the pathways involved. It is interesting to note that in the record shown in Fig. 4A, though the primary wave is visible only in traces 1 and 2, the later negative phase occurring 50 msecs. after the stimulus also appears in lead 3. It might be suggested that this later discharge represents a less well localized type of response similar to the secondary discharges described by Marshall and others. Before this may be accepted evidence is needed, and is lacking in the present records, to show that the spread is not a purely electrical effect, due to the size of the later discharge being greater than that of the primary wave.

Summary

1. Electrical stimulation of peripheral nerves in fourteen healthy subjects has produced potential changes on the scalp in twelve of them.

2. These potential changes occur over the contralateral sensory area, near the midline when stimulating the leg and more laterally when stimulating the arm.

3. The latency between the stimulus and the first peak of the response increases as the stimulus to the nerve is applied nearer to the periphery. It varies between 22 msecs. when stimulating at the elbows and 36 msecs. when stimulating at the knee.

4. Reasons are given for considering that these potential changes represent cerebral activity in the sensory area and are not artefacts.

5. The significance of the findings is discussed.

The author would like to express his indebtedness to the Engineer in Chief of the Post Office for the loan of the crystal oscillator used in these experiments, and to Mr. H. B. Law of the Post Office Research Station for advice in connexion with the frequency-dividing circuits used with this oscillator.

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For illustrations to this article see pages 134-136